LECTURES,

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LECTURES

ON SOME OF THE

APPLICATIONS OF CHEMISTRY AND MECHANICS

TO

PATHOLOGY AND THERAPEUTICS.

BY

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"And matter whatever it is must be held to be so adorned, furnished, and formed, that all virtue, essence, action, and natural motion may be the consequence and emanation thereof."

LORD BACON.

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PREFACE.

ON THE CONSERVATION AND CORRELATION OF ENERGY IN THE BODY.

The hypothesis of the constancy of the amount of force in the universe tends so much to promote experimental inquiry in every direction that for this, if for no other reason, it must be regarded as of the utmost importance.

No sooner was the relationship between the different forces of nature perceived than it was applied to the explanation of the action of all machines.

For the working of each mechanical, chemical, or electrical machine—for example, a mill, a steam-engine, or a telegraph —a source of power is necessary, and also provision for the application, direction, and control of that power.

The steam-engine will, perhaps, make the correlation of the forces and the controlling power most easily understood. The source of energy is the chemical attraction of oxygen for hydrogen and carbon. This force is latent until the particles of matter are brought sufficiently close to enable them to act the one on the other. Hence comes heat, and from the heat mechanical motion, and this partly resolves itself again into the agent from which it was produced. In addition to the motive power there is a regulating spring, a directing agency which gives or takes away oxygen or fuel, and by proper contrivances controls the motion of the machine.

In plants and in animals the same laws of the indestructi-

bility and the correlation of force offer a new and vast field for experimental investigation into the relationships of the forces that are in action; and promise to unfold much, though possibly not all, of the mystery that is comprehended under the word "life."

In the course of clinical lectures which I gave each year to the pupils whilst I was physician of St. George's Hospital, I constantly dwelt on the relations and differences between chemical and mechanical diseases.

Whenever I was able I pointed out a chemical or molecular disease running its course with scarcely any mechanical or massive disease resulting from it; but much more frequently I had to show how the molecular gave rise to the massive disease, how this again reacted on the chemical changes in the body, and these in consequence produced still greater mechanical results, until ultimately the motions of the diaphragm or heart were either stopped, or the patient was restored to a healthy state.

Thus, whenever a good case of diabetes was in the wards, I dwelt on the chemical nature of the disease and on the absence of mechanical symptoms; whilst in a case of gall-stone or renal-stone, I dwelt on the chemical error which led to the formation of the stone; then I pointed out the more serious mechanical disease resulting from the impaction, and then the wrong chemistry that this mechanical disease produced, the jaundice or uræmia, secondary chemical diseases of the blood and textures, far more dangerous than the primary chemical complaint.

When a case of uncomplicated apoplexy was admitted, I pointed out how the escape of blood in the brain caused mechanical pressure; whence came altered chemical actions of nutrition and oxidation (inflammation) set up to repair the injury and to restore the brain to a healthy state.

Or, if a case of chorea from fright was in the House, I dwelt on the resemblance of the symptoms to the effect of the electric shock, and I showed how the muscular action caused abnormal chemistry of secretion and nutrition, and sometimes led, even, to the stoppage of the heart.

Some of my lectures on Chemical Diseases were almost identical with some of my lectures on Animal Chemistry; and as a new edition of these has long been asked for, instead of reprinting them with the alterations which the progress of chemistry requires, I shall endeavour to give instances of a far more extensive application of chemistry to medicine. I shall do this by taking a few examples of errors of deficiency or of excess in the two great chemical processes of oxidation and nutrition, which, acting and reacting the one on the other, are always taking place in each particle of the human body during life. Thus, oxidation depends on the nutrition of the blood-globules, the heart, and the blood-vessels which admit of the diffusion of the oxygen and the fuel into each portion of the extravascular structures; whilst nutrition depends on oxidation not only directly but indirectly by the heat causing a relaxation of the vessels, and thus permitting an increased flow of nutritive substances to the parts.

I am far from supposing that animal chemistry at the present time is sufficiently advanced to admit of the classification of all diseases according to the altered chemical actions that are taking place in the body, and I shall not in the present course of lectures be able to give even a general view of the numberless variations that are already known to occur in the chemical processes of oxidation and nutrition.

But I shall endeavour to show, by a few striking examples, that the theory of the conservation of force opens a vast field of experimental inquiry, not only as regards the origin and connection of the actions which constitute disease, but also as regards the actions of the remedies by which those diseases are modified or removed.

It must be remembered that animal chemistry is only one hundred years old. The chemical actions of health, as in respiration, digestion, nutrition, secretion, are even now far from being thoroughly made out, although day by day our knowledge is advancing.

In proof of this I may take the first grand chemical action going on in the body—oxidation. How little of this do we know at present. Pettenkoffer's experiments on respiration

in health and in disease will probably give us for the first time accurate information on the amount of oxygen consumed by man in different circumstances. How does this oxidation take place? Whether the oxygen is made into the denser ozone (whose energy is to that of ordinary oxygen as common phosphorus to the allotropic red phosphorus)? Whether Schoenbein's views are correct—that every substance capable of being oxidised first makes the ordinary oxygen into ozone, and that this enters into combination, first slightly (still preserving its properties), and then firmly (when the ozone loses its characteristics)? Whether antozone exists, and by combining with ozone forms ordinary oxygen? These are questions which show how our knowledge is advancing, while they also show how much remains to be done before the chemistry of oxidation in the body can be thoroughly understood.

One two-thousandth part of ozone in the air is said to cause dangerous engorgement of the lungs, and even smaller doses long continued cause bronchitis and pneumonia. The blood of animals killed by ozone is found very rich in fibrin, and its dark colour shows that it has undergone active oxidation.

Professor Stokes thinks that cruorine (hæmatoglobulin) takes no part directly in oxidation, but that it so exalts the energy of the oxygen that it enables it in and out of the body to do what it could not do in its ordinary condition. However, the most energetic oxidations occur outside the capillaries, where no cruorine exists. Still, further, the modification of oxidation by the presence of substances in the blood and outside the capillaries is one of the problems of animal chemistry which M. Pasteur's work on fermentations out of the body may help us to solve. The resemblance of inflammation to ordinary combustion has long been recognised, and we are beginning now to see that fevers bear the same relation to inflammations that fermentations do to combustions. It is becoming clear that a vast class of diseases will be proved to be errors of chemical action—interferences caused either by want of regulation, or by the introduction from without, or by the generation within, the body of substances that increase,

diminish, or change the oxidation which is necessary for the working of the body.

Most probably among these simple errors of oxidation the following diseases will be found :—Diabetes, acidity; the production of oxalic acid, uric acid, uric oxide, cystine, fatty degeneration, gout, rheumatism, inflammation; and among fermentations, eruptive fevers, continued fevers, intermittent fevers, small-pox, syphilis, pyæmia, glanders, hydrophobia, plague.

If, instead of oxidation, I take assimilation, or the great chemical problem of nutrition, on which the repair of the body depends, it is easy to show that still more difficult questions await solution.

The quantitative and qualitative errors in the chemical composition of the different structures of the body are just beginning to be investigated, though but little at present is known of the causes on which these errors depend. The excess or deficiency in the supply of nutritive material—the wrong quality of the matter supplied—the wrong chemistry in the act of assimilation in the different textures—the excess or deficiency of chemical action in the removal of the used-up organs; these constitute a multitude of chemical diseases, some of which at present are known as hypertrophy, atrophy, and degeneration, and all of which chemistry will some day almost, if not altogether, explain.

In the following lectures I have separated for the sake of clearness the errors of chemistry in the repair of the body from the errors of chemistry in the oxidising action in the body; but a close relationship between these actions exists. Assimilation in great measure depends on the temperature of the body; a few degrees more or less may produce, as regards nutrition and oxidation, very different results; even the supply of nutriment to any part depends partly on the chemical action going on in that part, and by oxidation the used-up organs are made soluble or volatile to facilitate their removal from the body.

How far chemistry now is from dealing with these complex problems, or even with the more simple chemical questions of

the conversion of food into blood, and blood into textures, may be seen in the fact that the chemical action of simple substances, as arsenic, copper, mercury, lead, zinc, &c., on the blood and textures of the organs is not yet worked out.

Wherever it is possible, I shall point out how excess or deficiency of molecular action produces mechanical disease, and in my last lecture I shall rapidly prove that the converse relationship exists: for massive diseases or injuries give rise to secondary chemical diseases—that is, to excess or deficiency, or altered molecular actions which again react on the original mechanical wrong, whereby the secondary chemical actions are exalted or depressed.

He would, however, be but a poor physician who overlooked the influence of the nervous system either in the origin, the progress, or the treatment of every disease. The supply of oxygen and nutriment to every part is so immediately under the control of the nerves that act on the heart and capillaries, that the chemical processes of oxidation and nutrition can be accelerated or retarded by the action of the nerves quite as decidedly as by any direct chemical or mechanical action.

The progress of animal electricity will probably make clear the connection between nervous, electric, and chemical force. Then the large class of diseases which arise from the disturbances in the regulators of the chemical and mechanical actions in the body will be as clear as the errors in the chemical and mechanical actions themselves, which form the subject of this course of lectures.

We are just ceasing to regard the nervous force as the origin of all the power in the body. Instead of making it a creator of force, we now regard it as the liberator and restrainer of the force in the body; in other words, as the regulator, through the heart and blood-vessels, of the extent and degree of oxidation and nutrition that occurs in the human machine.

Taking the various parts of the nervous system separately, there are—1st, central organs; 2ndly, conducting organs, transmitting impressions at the rate of twenty-eight or

twenty-nine yards a second; 3rdly, sense organs; and, 4thly, peripheral working organs; and it is in these that the regulating power is made manifest. For example, mechanical, chemical, electrical irritation of the vagus stops the heart's action. Irritation of the sympathetic or division of the vagi increase the frequency of the heart's contraction. The ganglia of the heart seem to differ in their action. Experiments show that some have a liberating action, an automatic rhythmic action; while other ganglia have a restraining action. Another example is seen in the vaso-motor nerves. Both Bernard and Schiff consider that these are of two kinds—the one set closing the vessels and the other set of nerves opening them. When closed, the blood is stopped; there is paleness and coldness, and no effusion of parenchymatous fluid: when opened, there is increased flow of blood, redness, and higher temperature, and increased exudation from the capillaries. In other words, the mechanical and thermal actions in the body are regulated by the nervous force acting on the heart and blood-vessels.

The difference between muscular and nervous action is that between the horse and his rider, the gun and the gunner, the steam-engine and the driver; and it would not be more wrong to attribute all the force in these machines to the action of the spur and bit, the trigger, or the lever, than to attribute the force of the muscles to nervous action.

The finger of the engineer liberates the power stored up in the boiler; and the nerves unlock forces, already latent in the muscles. But besides those forces which result in the mechanical and other motions of the formed body, there are others to which the body owes its form, and which manifest themselves most wonderfully in the first stages of the embryo's existence. Animal form lies latent in the substance that forms the first animal cell. It is the power resident in this substance which determines the cycle through which the matter it draws towards it is to run.

For the last century Physiology and Medicine have been chiefly occupied with the determination of the structure of the organs of the body in health and disease; even up to the

present time the microscopical variations in the form and substance of the different parts of the body yield remarkable discoveries; but the inquiry into the conservation of energy in the body promises results which will unfold the mystery of health and of disease.

We have ceased to look on the human machine as a creator of vital or nervous force, and we are beginning to regard it as a converter of latent into active force.

In the body the force is latent in the elements, oxygen, hydrogen, carbon, nitrogen, sulphur, phosphorus, &c. The amount in each pair of elements may be measured by the heat produced in combustion or by the mechanical work that can be done by that heat. Thus, in the combustion of one gramme of hydrogen, the caloric equals 34462 units—a unit being the quantity of heat that raises 1 gramme of water from 0° to 1° C.—whilst in the combustion of one gramme of carbon the caloric equals only 8080 units; the mechanical work can be calculated from the fact that the mechanical equivalent of each unit of heat is equal to 425 grammetres—(that is, the work of raising 425 grammes one metre high). Hence the work that can be done by one gramme of hydrogen is 14,818,660 grammetres, and by one gramme of carbon 3,474,400 grammetres. As the number of units of heat produced in the body daily amounts to many millions, it is convenient to make the unit 1000 times greater, namely, the heat required to raise one kilogramme of water from 0° to 1° C. The mechanical equivalent then becomes 425 kilogrammetres.

Mr. Joule makes the mechanical equivalent of heat 772 foot pounds—that is, the quantity of heat required to raise one pound of water one degree of Fahrenheit is equal to the heat produced by a weight of one pound of water falling 772 feet. It would raise a pound weight 772 feet high, or 772 lbs. one foot high. As yet, approximations only can be made to the amount of force that daily goes into the human body in the food and oxygen. As with the matter, so with the force of the food: the quantity that goes in is balanced by the quantity that comes out in any given time, provided

the force and matter in the body at the beginning and end of the time is the same.

M. Barral has given an approximate estimate of the different amounts of force lost in different ways. From 1 to 2 per cent. of power is given out in the heat of the urine and fæces; from 4 to 8 per cent. in the heat of the breath; from 20 to 30 per cent. in evaporation of water from the surface; and from 60 to 75 per cent. in conduction and radiation, and in mechanical work.

Force enters the body latent in the food and air. It consists of the affinities, as yet unsatisfied, which subsist between the constituents of the food and the respired oxygen. In the body, these affinities come into active play, producing heat, mechanical motion, and all those other actions, internal and external, to the sum of which we give the name of life.

Death is the stoppage of this conversion of latent force into active force, caused either by some arrest of action in the heart, lungs, or brain, or by some direct interference with the chemical actions in the ultimate molecules of the organs.

When the number of centuries during which natural knowledge has been studied shall have approximated to the number already spent on classical knowledge, we may expect that the changes in the matter and force in the body in health and in disease will be so well known that even mental diseases will be more thoroughly understood than the simplest of those chemical diseases which, as far as our present knowledge admits, I shall endeavour to make clear to you in this course of lectures.

In my clinical lectures I tried to point out clearly the difference and relationship between the chemical and mechanical treatment of disease, to show that sometimes only chemical remedies are wanted; in other cases, more especially in Surgery, that mechanical treatment alone need be used; but that most frequently both chemical and mechanical actions are simultaneously wanted, and that these react potently on one another. For example, medicine with rest will do what medicine without rest will not; or diet and exercise may do together what either separately could not

effect. The mode of action of mechanical remedies is at present much more comprehensible than that of chemical remedies. Motion increases chemical action, and rest checks it. When the blood is carried through a muscle at rest the quantity of oxygen remaining in the blood is nearly $7\frac{1}{2}$ per cent., but if the muscle is in motion then the quantity of oxygen is reduced to $1\frac{3}{10}$ per cent. In other words, when motion takes place there is much more chemical action than when the muscle is at rest.

Motion in two ways increases chemical action—1st, directly by conversion of force, and, 2nd, indirectly by bringing the molecules more closely into contact, so that the latent energy can be changed into active force. This is chiefly effected by the circulation bringing fresh and larger amounts of oxygen in contact with the hydrogen and carbon, phosphorus and sulphur of the textures.

Rest lessens the supply of oxygen, lessens the pressure in the capillaries; lessens the mixture and contact of molecules in the textures, and thus diminishes chemical action.

Heat and cold act both chemically and mechanically in promoting or checking chemical action. Heat acts directly by conversion of force; it also probably acts by dilating the small arteries and veins, and thus permitting freer circulation, and the consequent increased chemical action.

Cold acts directly by stopping chemical action, and indirectly by constricting the small arteries and veins, and thus hindering the circulation and preventing the contact of the oxygen with the combustible and nutritive substances.

Food acts both chemically and mechanically,—chemically, 1st, by furnishing latent force, and, 2nd, material for the formation of the organs by which that force is made active. It acts mechanically by the solid parts increasing chemical action in the stomach, and by the fluid parts adding to the mass of liquid in the blood and by the dissolved solids that pass into the blood, adding to its specific gravity, and thus altering the osmotic actions throughout the system.

Food may be divided into water, salts, carbonaceous and nitrogenous matters. The water and salts do not take a

direct part in oxidation and nutrition, but they are indispensable indirectly to the chemical actions by dissolving the active substances and bringing them into sufficiently close contact for the action to take place. Both carbonaceous and nitrogenous aliments can be acted on by oxygen, and can thus change their latent into active force.

Hydrogen, carbon, and nitrogen, sulphur, phosphorus, iron, and lime, enter into the composition of the organs by which the conversion of latent into active force is effected. Ultimately, more or less completely, these elements are themselves acted on by the oxygen, and thus no distinction exists between respiratory and plastic food. Professor Liebig's division of food, however, gave the first impulse towards the clear comprehension of the two great chemical actions of oxidation and nutrition that take place in each particle of the body; I hope to prove to you that extreme variations of these actions constitute disease.

PART I.

LECTURE I.

ON THE CHEMICAL CIRCULATION IN THE BODY.

All our knowledge usually passes through three stages as it advances to perfection. First, a stage in which we think we know everything; then a stage in which we find we know nothing; and, finally, a stage in which we rapidly obtain those clear and connected ideas in which all sound knowledge consists.

As regards the absorbent system of animals and the mode of action of remedies, we have long been in the first or second stage, and in this lecture I intend to show you that there is reason for believing that in regard to these subjects we are about to enter on the third stage; for that, in addition to the circulation of the blood, there is the dawn of another or chemical circulation, dependent in part on the mechanical circulation, but carried on mostly by diffusion from the blood into the textures, and from the textures into the absorbents, which thus become necessary agents for performing those actions of oxidation and nutrition on which, in great part, animal life depends.

Mr. Huggins has lately proved that the spectrum-analysis can determine the chemical composition and the physical constitution even of substances outside those circulating bodies that constitute our solar system. And by the same spectrum-analysis, the minutest particles of foreign substances can be traced passing into those parts of the body which are most distant from the circulation of the blood.

In the human body the laws of diffusion modified by pressure determine the passage of all substances from the stomach into the circulation, from the circulation into the textures, and from the textures or circulation into these excretions. To Mr. Graham we owe the investigation of these laws of diffusion of gases and liquids; and the division of substances into crystalloids and colloids. One or two experiments, and for them I am indebted to Mr. Ansell and to Mr. Graham, will make the meaning of these terms more clear to you. Inside and outside this porous cell there is at present atmospheric air. There is no passage of the outer air into the inside of the cell, nor of the inside air to the outside of the cell; but if hydrogen is put outside, being lighter than common air, it rapidly passes into the inside of the cell, whilst the heavier air inside more slowly passes out; and thus pressure is produced inside the cell, and the index shows how much pressure exists. So also with this india-rubber ball. When the gases inside and out differ, the lighter gas will pass rapidly in, and such an alteration of form will occur that a spring will be liberated and this bell will say that light gas has passed through the india-rubber ball. Mr. Ansell has invented this test for the explosive gas in coal-mines, that it may ring its own alarm. In these two glass vessels the same excess of diffusion of the lighter over the heavier gas is shown, but the action has taken place more slowly. Originally over both jars the india-rubber was flat. But through this concave india-rubber the hydrogen has more rapidly passed out than the air has passed in; and through the other convex rubber the hydrogen has more rapidly passed in than the atmospheric air has passed out.

So with these liquids, for which I am indebted to Mr. Graham. Here is a very diffusible crystalloid substance, acetate of rosaniline, or magenta; and in this other vessel there is a much less diffusible or colloid substance, cochineal. In half an hour you will see the crystalloid will pass through the membrane, whilst the colloid will show no signs of passage.

Here is another semisolid contrast. In the one jar there

is bichromate of potash in gelatine above, with pure gelatine below; and in the other cochineal in gelatine above and pure gelatine below: the bichromate diffuses, whilst the cochineal is unmoved.

The same laws of diffusion modified by pressure determine in the body the passage of substances from the stomach into the circulation, from the circulation into the tissues or ducts, and from the tissues back through the absorbents to the circulation.

The circulation of the blood cannot be represented by the stem of a tree curled round on itself, but rather as a series of circles formed by each terminal branch-twig joining a terminal twig of the root. The enormous number of these terminal circles may be seen in any injected preparation of any part of the body. The whole substance seems to consist of these vessels alone. The walls of these vessels are of the finest membrane, through which diffusion takes place with the greatest rapidity into the tissues beyond the circulation. These tissues constitute the different organs of the body, nerves, muscles, glands, ligaments, bones, &c. Each particle of each nerve, muscle, or gland, is encompassed by blood-vessels on which its growth and its action depend; but there are some few spots in the body where blood-vessels would be dangerous to the function of the part. These parts may be regarded as outside that circulating system which binds together the rest of the body.

The most numerous of these extravascular structures are the cartilages of the joints; and at a far greater distance may be placed the most remarkable structures of our body, the crystalline lenses which, without any circulation of their own, are separated from all circulation by an aqueous and glassy fluid, which themselves also have no circulation. The lenses then might well be thought to be altogether free from all the multitude of disturbing substances that enter through the stomach into the circulation of man. By this model of an eye, perhaps, you will best realize the distance of the lens from the circulation of the blood.

The lenses, the humours of the eye, and the cartilages of the joints, thus constitute the parts of the textures most

distant from the vessels, whilst the proper tissues of the various organs of the body constitute the parts of the textures most immediately touching the circulation. The absorbent system and the ducts of glands constitute the drains by which substances that have passed out of the circulation into the textures are taken up into the circulation again or pass out of the body.

It has long been known that bile would diffuse into every texture; that madder would diffuse into the bones and into the fœtus, and urate of soda into the joints; carbazotic or picric acid into the skin; mercury into the gums; lead into the gums and muscles, and silver into the skin; and it has long been known that multitudes of substances would run through the stomach into the circulation and out through the textures into some of the excretions. Ether, asparagus, turpentine, and many other such substances require no mention here.

It occurred to me that both in animals and in plants* the spectrum-analysis ought to determine with certainty where diffusing substances go to; how long they are in going out of the stomach into the textures; how long they stay in the textures, and how quickly they cease to appear in the excretions; and, with Dr. Dupré's help, a long investigation into the rate of passage of crystalloids into and out of the textures of the body was undertaken.

The delicacy of the spectrum-analysis may be seen in this table, which gives the smallest quantity of each substance that can be thus detected:—

Chlorate of soda . . .	$\frac{1}{195}$ millionth of a grain.
Carbonate of lithia . . .	$\frac{1}{8}$ „
Chloride of strontium . .	1 „
Chloride of barium . .	1 „
Chlorate of potass . . .	$\frac{1}{65}$ thousandth of a grain.
Chloride of lithium . . .	$\frac{1}{12}$ millionth of a grain.
Chloride of rubidium . .	$\frac{1}{16}$ thousandth of a grain.
Chloride of cæsium . . .	$\frac{1}{125}$ „

* Cress sown on paper, when one inch high had the paper moistened with water containing a little chloride of lithium; in ten minutes and twelve minutes the lithium was detected in the leaves.

Soda exists everywhere, and in everything we eat and drink; so there was no use in looking for soda in the circulation and textures, for it was sure to be there.

Lithia exists in many vegetable and animal substances, according to the soil on which they grow or live. Here is a table of substances which we examined for lithia:—

In potatoes—seldom found	In tea—slight traces
apples—sometimes	coffee—slight traces
bread—traces	ale—slight traces
cabbage—distinctly	porter—slight traces
Rhine wines—always	mutton—none
French wines—distinctly	beef—none
Sherry—distinctly	milk—none.
Port—distinctly.	

It had already been found—

In sea water
kelp
spring water sometimes
ashes of wood grown in the Odenwald
Russian and other potashes
tobacco
vine leaves and grapes
ashes of the produce of the fields in the Palatinate
milk of animals eating the produce
ash of human blood and muscle
meteoric stones
all the drinking waters of London.

The spectrum of lithium is very characteristic and very perceptible, and some approximation to a quantitative determination may be arrived at by observing the amount of substance that requires to be burnt to obtain the reaction, and by the necessity, in some cases, for the removal of interfering substances previous to the combustion. Thus three degrees may readily be observed. The highest amount of lithia is present when each particle of the substance introduced into the flame gives the lithia reaction; and a smaller amount of lithia is present when the whole of a lens or of an organ must be extracted with water to remove the lithia previous to the combustion; and the smallest trace is present when the substance has to be incinerated, the ash

treated with sulphuric acid, the excess of acid driven off, the dry residue extracted with absolute alcohol, the alcohol evaporated, and the dry residue tested. These three quantities may be designated as the slightest trace, a trace, and plenty.

As soon as experiments on man and animals showed that the infinitesimal quantities taken in with the food were rarely to be perceived in the textures, experiments were made to determine how quickly the lithium diffused from the stomach into the blood circulation, and from the circulation into the textures, and whether it was to be found in those distant parts of the textures where no circulation existed, and especially in the lens of the eye.

The following table gives the experiments made on the rate of the passage of chloride of lithium from the stomach not only into the circulation, but out of the circulation into the textures of a guinea-pig.

After $1\frac{1}{2}$ grain was taken.	In 3 days	plenty was found everywhere.
3 „	15 minutes	everywhere except in the lens.
3 „	30 „	„ „
3 „	30 „	„ traces in the lens.
3 „	30 „	„ outer part of the lens.
3 „	60 „	„ „
3 „	60 „	„ except in the lens.
3 „	in $2\frac{1}{4}$ hours	„ and throughout the lens.
3 „	4 „	„ „
3 „	8 „	„ „
3 „	24 „	„ „
3 „	26 „	„ „
$\frac{1}{4}$ „	$5\frac{1}{4}$ „	„ except in the lens.

It follows from these experiments that three grains of chloride of lithium given on an empty stomach, may diffuse into the cartilage of the hip-joint and into the aqueous humour of the eye in a quarter of an hour. In very young and very small pigs, the same quantity of lithium may in 30 or 32 minutes be found in the lens of the eye, but in an old pig in this time the lithium will have got no farther than the humours of the eye. If the stomach was empty when the chloride of lithium was taken, then in one hour the lithium may be very evident in the outer part of the lens, and very faintly

in the inner part; but if the stomach be full of food the lithium does not in an hour reach the lens. Even in two hours and a half the lithium may be more marked in the outer than in the inner part of the lens. In four hours the lithium will be in every part of the lens, but it will still be more evident in the humours than in the lens. Even in eight hours the centre of the lens may show less than the outer part. The lithium will be found in as great quantity in the centre of the lens as in the outside after twenty-six hours.

When instead of being put in by the stomach, the lithium was injected into the skin: three grains of chloride of lithium in 24 minutes showed the lithium in the lens and in every texture; in 10 minutes, slightly in the lens; but plenty everywhere else; in 4 minutes no lithium was in the lens, but plenty in the aqueous humour of the eye and in the bile; one and a half grain in 5 minutes showed no lithium in the lens; but plenty in the aqueous humour and in the bile.

Having thus shown that lithium will pass everywhere into the textures in between 4 and 15 minutes, when injected into the circulation, and between 15 minutes and 26 hours when taken in by the stomach, some experiments were made to determine after how many days the lithium ceased to be detected in the textures after it had been taken. Usually three pigs were taken: to one no lithium was given, the second was killed in a few hours after a dose of lithium, and the third was given the same dose and killed after many days.

The following table shows the rate at which chloride of lithium passes out of the textures:—

2 grs. in 6 hours gave plenty everywhere.	In 6 days gave no trace in the alcoholic extract of the kidneys, livers, or lenses.
2 „ — „	„ „ „
2 „ — „	In 4 days gave none in the lens.
1 gr. in $5\frac{1}{2}$ hours showed partly in the lens.	In 3 days gave faint traces in the lens.

It follows from these and other experiments that twice in six days, and once in four days two grains of chloride of

lithium, which in six hours gave lithium everywhere, in six days ceased to be detectable in the lens, and that even in three days the lithium is most probably diminishing in the lens.

Having thus gained a clear knowledge of the time it takes for a small quantity of lithia to pass in and out of the textures of an animal, I proceeded, through the kindness of my friends Mr. Bowman and Mr. Critchett, to trace the passage of lithium into that part of the body which is most distant from the blood circulation in man. Lithia water is by no means an unpleasant drink, and a few minutes, or a few hours, or a few days before the operation for cataract, twenty grains of carbonate of lithia dissolved in water were taken.

No less than seven cataracts were previously examined with the greatest care, to determine whether lithia was usually absent, and in only one instance was the very faintest trace of lithium detectable.

The following table shows the rate of passage of carbonate of lithia into and out of cataracts—

20 grains of carbonate of lithia were taken

25 minutes		before the operation	—No trace of lithium was found in the cataract.
2½ hours		,,	—Lithium in the watery extract of the cataract.
3½ ,,		,,	—Lithium in each particle.
4 ,,		,,	,, ,,
4¼ ,,		,,	,, ,,
4½ ,,		,,	,, ,,
5 ,,	(old man)	,,	,, ,,
5 ,,		,,	,, ,,
7 ,,		,,	,, ,,
4 days	spontaneous soft cataract, 25 to 30	,,	—Traces in alcoholic extract of ash.
7 ,,		,,	—In alcoholic extract not the slightest trace of lithium.
7 ,,	5 hours	,,	,, ,, ,,
7 ,,		,,	—Slightest trace in the alcoholic extract.

It follows from these experiments, that in the human body twenty grains of carbonate of lithia taken into the stomach in

two and a half hours will have partly passed into every particle of the textures and beyond the blood circulation even into the most distant parts, and in three and a half hours it will be distinctly present in each particle of the lens.

After four days it will still be distinctly present in each particle of the lens.

After five days it will have begun most clearly to pass out of the lens, and in seven days scarcely the smallest trace will be detectable there. The most striking experiment was in the case of a young girl with two soft cataracts. She took twenty grains of carbonate of lithia, and in seven hours one lens was removed, and the smallest particle of the lens showed the presence of lithium. The other cataract was not removed for seven days after the first operation; then not the slightest trace of lithium could be found in the lens.

A long series of experiments on the passage of lithium out by the excretions, after it had been taken in by the mouth, showed nearly the same fact, namely, that after a dose of twenty grains, the lithium was not entirely thrown out of the body under six, seven, or eight days.

Thus, then, both in animals and man the same law obtains. A single dose of lithium in a few minutes passes through the circulation into all the ducts and into every particle of the body, and even into the parts most distant from the blood-circulation.* There it remains for a much longer time than it took to get into the textures, probably for three or four days, varying with the quantity taken; then it diminishes, and finally, in six, seven, or eight days, the whole quantity is thrown out of the body.

In animals it is very difficult accurately to determine the time when a single dose is removed; for a portion passes out in the perspiration and gets into the hair, and the animal thence re-doses itself with the lithium which had already passed through the blood-circulation into the textures and out by the perspiration, and this re-dosing may be continued over and over again, so that even for thirty or forty days,

* When seven grains of carbonate of lithia were given eight hours before delivery, the lithium was detected in each particle of the umbilical cord.

after a dose of three grains, some lithium may be detected in guinea-pigs still passing out of the body.

Having thus traced the lithium in and out of the textures the question of far greater importance remains—What does the lithium or other alkaline salt do whilst it is in the textures? In other words, What is the action of alkalies in the system? What is the action of carbonated alkali at a temperature of 38 C. (100 Fahr.) when oxygen at the same time is present, on 1st, organic acids; 2nd, neutral hydrocarbons; 3rd, fatty matter; and 4th, albuminous substances?

The most remarkable instance of the action of alkali when organic acid and oxygen are in contact is in the decomposition of pyrogallic acid. In this vessel I have oxygen and pyrogallic acid in contact, and no action takes place, and none would take place if alkali were not added; but immediately on the addition of potass, action begins, the pyrogallic acid is unable to keep its composition, and is burnt by the oxygen aided by the alkali. More stable acids of lower composition are produced, and these combine with the alkali and liberate carbonic acid. If carbonated instead of caustic alkali be used, the action is not nearly so rapid or complete as with caustic alkali.

The best example of the destruction of a neutral hydrocarbon by oxygen aided by alkali is in the reduction of oxide of copper by sugar. The metallic oxide furnishes the oxygen, the alkali assists the formation of acid from the sugar, and draws it out of the sugar, destroying the neutral compound.

In fatty matters the alkali splits the fat into fatty acid and glycerine, and forms a soap with the acid. Oil of bitter almonds exposed to common oxygen or ozonized oxygen absorbed in two hours two cubic centimetres of oxygen; with carbonate of soda it absorbed in the same time 2,75 CC. When mixed with an alcoholic solution of potash, and heated benzoic acid combines with the potash, and the whole contents of the tube solidify; the alkali causes the oxidation of the oil; and by extreme oxidation carbonic acid and water would be the final results.

The action of alkali and oxygen on albuminous substances at low or moderate temperature, 100 Fahr., has not been yet studied. At high temperatures with alkali the entire decomposition of the substance with the production of carbonic acid and ammonia, and a multitude of less perfect products of oxidation have long been known; the same substances oxidized at a higher temperature without the presence of alkali give rise to fewer intermediate products, and to a greater amount of the ultimate products of oxidation, *viz.*, water, carbonic acid, and ammonia, out of which the albumen was originally formed.

M. Béchamp stated that by the oxidation of albumen by manganic acid urea was produced, but this proved to be benzoic acid; and probably kreatin, uric acid, urea, and other products will not be obtained from albuminous substances until we follow the method of oxidation that occurs in the body, *viz.*, a temperature of 38 C. (100 Fahr.), a moderately strong solution of carbonate of soda and basic phosphate of soda, and the action of oxygen possibly in an ozonized state.

Von Gorup Basanez (Liebig's 'Annalen,' vol. cx. p. 86, and cxxv. p. 207) has traced the action of ozone at ordinary temperatures on a multitude of animal and vegetable substances, but of these my time allows me to mention only one or two striking examples.

Cane or grape sugar when in contact with ozone undergoes no change, but where grape sugar is exposed to ozone with potass, soda, or carbonate of soda, it is entirely oxidized, and carbonic and formic acids only result. When no alkali is present no action occurs. Cane sugar oxidizes with alkali and ozone much slower than grape sugar.

Olein is quite inactive when exposed to ozone, but with potass or carbonate of soda the olein is immediately oxidized. The olein is saponified and the glycerine is oxidized into acrolein and ultimately into carbonic, formic, and propionic acids. The oleic acid is much more slowly oxidized into formic and carbonic acid.

Hence the action of alkalies out of the body on the different classes of substances of which we are built up is

sufficiently clear. The alkali disturbs the equilibrium of the elements in the organic body by its affinity for acids. Aided by oxygen and heat, more or less complex acids are formed from the neutral substances, and if the action of the alkali is sufficiently continued, carbonic acid, water, and ammonia alone remain.

The progress of therapeutics probably depends on the application of our knowledge of the action out of the body of different medicines on the different chemical constituents of the body, to the explanation of the action of the same substances on the components of the textures in the body.

I have shown you how alkali out of the body promotes oxidation. The chemist can have no doubt that the same action takes place in each particle of the textures to which the alkali is carried. Thus carbonate of lithia, soda, and potass, lime, magnesia, rubidium, cæsium, are indirectly oxidizing agents, increasing chemical action in the different substances of which the textures are composed, according to the amount of the different alkalies that can diffuse into the textures, according to the different properties of the substances capable of oxidation that happen to be in the textures, and according to the amount and active state of the oxygen present and the amount of heat that assists the action, and according to the facilities for the removal of the products of the combustion.

Chloride of rubidium and cæsium we have proved to follow the same law as chloride of lithium, in that these substances pass into the crystalline lens, and can be detected there ; but the evidence is much less distinct than in the case of lithium, so that the rate of the passage of these substances in and out of the textures cannot so easily be determined. Twenty grains of chloride of rubidium, and the same quantity of chloride of cæsium were necessary to give traces of the spectrum reaction for these substances in the lenses of guinea-pigs.

There can be no reasonable doubt that as alkalies pass in, so we shall prove that vegetable acids, if not stopped by the alkaline fluid that is contained in the circulation, will pass

into every particle of the textures, and when there these acids must have exactly the reverse action to alkalies. By lessening the alkalescence of the serum and tissues, vegetable acids must tend to stop the oxidizing process.

As starch, sugar, and alcohol may be looked upon as becoming in the body vegetable acids, there is here a vast field for research, for there can be no doubt that the sugar and alcohol of our food pass at least as quickly as alkalies into the vascular and non-vascular textures of our bodies.

How far mineral acids can penetrate into the textures cannot be determined, and it may well be doubted if they reach the textures at all, although, by rendering the blood less alkaline, they must indirectly render the diffusing fluid in the textures less alkaline also.

Alkaloids we hope to detect diffusing into the textures in the same way, if not at the same rate, as alkalies. How they act on the different components of the textures of the body, chemistry at present has not determined. The action of alkaloids on sugars, fatty matters, and albumen at first sight appears altogether unproved. There exists in the brain and nerves a substance discovered by Dr. Oscar Liebreich, and named by him protagon ($\mathrm{C}_{116}\mathrm{H}_{241}\mathrm{N}_4\mathrm{O}_2\mathrm{P}$). It gives rise to neurin ($\mathrm{C}_5\mathrm{H}_{13}\mathrm{N}$), glycerin-phosphoric acid, and a fatty acid, when treated with alkali; and this substance, of which $\frac{1}{10000}$th forms a strong jelly with water, may be acted on by the alkaloid, and thus form a nerve substance, having very different physical and chemical properties from the protagon in its unaltered state.

Even the action of ammonia in the different tissues of the body is not yet made out. In the 'Phil. Trans.' part ii., 1851, p. 409, I have shown that in passing through the stomach into the blood, or when in the blood, ammonia is partially oxidized, and that the same oxidation happens when urea is taken, and probably when caffein and the alkaloids pass into the blood, but the action that occurs as soon as ammonia, urea, or alkaloids come into contact with the different substances in the different textures, and the rate at which these alkaloids are ultimately oxidized in the textures,

has yet to be determined. The first effect of alkaloids is to increase chemical action; but the resulting chemical combinations that take place, and the alterations in the textures that are produced by ammonia, urea, and alkaloids are at present undetermined. Moreover, the alterations these substances occasion in the products of decomposition of the tissues, whilst being themselves finally decomposed and removed from the body, are still entirely unknown.

Judging from the action of alkalies, there can be little doubt that alkaloids in a few minutes diffuse into every texture, and act according to their powers on the different substances with which they come into contact. If our means of analysis were sufficient, they would be found probably for three or four or more days in the textures, generally much longer than the symptoms, which depend upon contrast, would lead us to expect.

Lastly, we have proved that some salts of the metals diffuse like chloride of lithium into every texture of the body. Three grains of sulphate of thallium we have followed in twenty-two hours into the crystalline lens, and into the cartilages, the nerves, the liver, and the kidneys. It may be doubted, perhaps, whether thallium is a metal; but the same fact we have also determined to be true of sulphate of silver. The silver being detected by a very delicate galvanic arrangement.

In twelve days a grain and a quarter of sulphate of silver was given to a guinea-pig. The ashes of the liver, kidney, and stomach showed silver fairly. The ash of the bile showed it rather less distinctly. The ash of the lenses showed only very slight traces of silver, but silver was there. The ash of the brain showed no silver.

And here again a vast field for inquiry is opened. What is the action of the metallic salts on the water, salts, hydrocarbons, fats, albuminous substances of which each tissue is built up? How do the metallic salts influence the oxidation and nutrition going on in the textures? The power of the salts of silver, lead, and mercury, &c., to form insoluble or soluble compounds with albumen out of the body seems to indicate the action of these substances on the albuminous

matter in the body. A compound with the albumen may be formed which may check the action of the organ, or the metal may be reduced or form a sulphuret, as with silver salts; and may be deposited in the textures and there remain, rendering the organ useless, as with lead salts; or the metallic salt may set up a more active chemical change in the albuminous textures or substances with which it is brought into direct contact, and this chemical action may rise to that degree which is known as inflammation; and the salts of mercury may be taken as examples of substances possessing this action.

From this view of the rapid passage of crystalloid substances into the vascular and non-vascular textures of our bodies, there arises a feeling of surprise that under such constantly varying conditions, the different functions of the different parts can be carried on. There is, however, from these experiments, but little room to doubt that crystalloid substances like water, alcohol, salt, and sugar, assisted by the mechanical circulation of the blood, can in a few minutes pass by diffusion into each particle of our textures; and if in them these substances must take part in the changes of matter and force that are proceeding there, according to the amount of substance that enters in, according to the chemical properties that the substance possesses, and according to the conditions and times during which the action proceeds.

Thus, this circulation of diffusion rises even to an equal if not to a greater importance than that other more mechanical circulation of the blood, which indeed, in two out of the four grand divisions of animals, is almost absent, and during the early weeks of our own fœtal life is entirely wanting; and in this chemical circulation we recognize a link between the lowest vegetable and the highest animal creation, since this diffusion is a necessary condition on which the chemical actions in both kingdoms of nature depend.

To sum up then, I have tried to show you that there are good grounds for believing that there exists within us, in addition to the mechanical or animal circulation of the blood, another, and a greater and a more strictly chemical circulation,

closely resembling, if not identical with, that which obtains in the lower divisions of animals and in vegetables. A circulation in which substances continually pass from the outside of the body into the blood, and through the blood into the textures, and from the textures either into the ducts, by which they again pass back into the blood, or are thrown out of the body, or into the absorbents, by which they are again taken back into the blood, again to pass from it into the textures.

This chemical circulation leads directly to two most important inquiries:—First, whether substances that diffuse into this larger circulation act as they would do out of the body under somewhat similar circumstances upon the different substances with which they come into contact in the different textures; either promoting the formation of new compounds, or giving rise to decompositions in the substances that are present in the tissues.

And, secondly, whether the chemical force, which may have been latent for ages in the mineral and vegetable substances that can enter by our vegetable and mineral food and medicine into this larger circulation, may be so given out in the textures as to increase or diminish those actions of oxidation, motion, sensation, and nutrition, which almost, although not altogether, constitute that assemblage of correlated actions which we sum up in two words—Animal Life.

LECTURE II.

ON THE EXISTENCE IN THE TEXTURES OF ANIMALS OF A FLUORESCENT SUBSTANCE CLOSELY RESEMBLING QUININE.

In my first lecture I brought to your notice the fact that "a single dose of lithium in a few minutes passes, through the circulation, into all the ducts, and into every particle of the body, and even into the parts most distant from the blood circulation, and then I showed you that it remains there for a much longer time than it took to get into the textures (probably for three or four days, varying with the quantity taken), and that then it diminishes, and finally, in six, seven, or eight days, the whole quantity is thrown out of the body."

No imagination could have anticipated that this line of research into the rate of passage of substances into and out of the textures would lead to the supposition that man and all animals possess, in every part of the body, the most characteristic peculiarity of the bark of the cinchona trees of Peru.

After determining the rate of passage of lithia and other mineral matters into and out of the body, Dr. Dupré and I proceeded to endeavour to trace the rate of passage of quinine into and out of the textures of animals.

We chose quinine because of that splendid test which led Professor Stokes to the discovery of the change of refrangibility of light.

Here, for example, are different solutions of quinine of different strengths, and by means of the production of fluorescence in the electric light, you see how we can de-

termine which of these solutions contains the greatest quantity of quinine; and by forming standard solutions it would be easy to measure how much quinine existed in each of these solutions. Moreover, Professor Stokes discovered that when a solution of common salt was added to this quinine solution, the fluorescence entirely disappeared. Though this may be so in sun-light, it is not so in this electric light; and, moreover, on adding a solution of sulphate of soda to a solution of chloride of quinine, the fluorescence, as you see, is greatly increased.

Still further, Professor Stokes showed that one solution of quinine entirely stopped these rays from passing into a second solution of the same substance, so that you might almost tell whether you had a solution of quinine by seeing whether it cut off the fluorescence from a second solution of quinine.

Our first object was to determine the delicacy of this reaction for quinine. We arrived at the following results, when the spark from a Ruhmkorff coil was the source of light:—

Sulphate of quinine	gave	slight fluorescence	when	$\frac{1}{360000}$	of a gr.	was present.
”	”	feeble	”	$\frac{1}{330000}$	”	”
”	”	distinct	”	$\frac{1}{250000}$	”	”

One grain of sulphate of quinine in one million eight hundred parts of water showed the blue fluorescence distinctly in 20 grs. of the solution. In another experiment, the same amount of quinine in one million four hundred and forty-four parts of water showed fluorescence very distinctly.

Having thus got our test, we proceed to apply it to determine the passage of quinine into and out of the textures of guinea-pigs.

A guinea-pig was given quinine, and for comparison another guinea-pig was killed at the same time, having had no quinine.

In the pig that had taken quinine, each organ was heated in a water-bath, with very dilute sulphuric acid. This extraction was repeated over and over again. The acid extracts

were mixed and filtered after cooling, neutralized with caustic soda, and repeatedly shaken up with their own bulk of ether. The residue left after evaporation of the ether was taken up by dilute sulphuric acid, filtered, and tested for fluorescence.

The pig that had taken no quinine, had each organ treated in a precisely similar way. To our great disappointment, at first, we found that not only had the pig that had taken quinine a fluorescent substance in the textures, but that an almost exactly similar substance was extracted from the organs of the pig that had taken no quinine. Every texture was examined, and in every one this fluorescent substance occurred.

We then endeavoured, in every possible way, to find a means of separating the natural from the induced fluorescence. And as every method failed, and we were compelled to recognize the close similarity of the substance that exists in the textures to quinine itself, we for a time dropped the original inquiry, and proceeded to a more complete investigation of the natural fluorescent substance in animals.

Without any preparation this substance can be shown to exist in the living and in the dead textures. There is one transparent substance which is, above all, most suited for this inquiry.

Here are some lenses removed from the eyes of bullocks, guinea-pigs, and man. You see how clear, white, and transparent these substances are; and if I take a bullock's eye, which by gentle pressure has been flattened so that the structure can be distinctly made out, there is plainly no colouring matter. As in quinine, nothing is seen until the blue rays of the electric light fall on the lenses; then look at the splendour of the reaction. Here, with the guinea-pig's lenses, the same is seen; and here, with the flattened bullock's eye. You might be tempted to think that this is a *post-mortem* change, a result of decay; but here is a fresh bullock's eye, look at this blaze of bluish-green light; but still more full of suggestion is an experiment with a dilated pupil in a

living animal or in man. Let me show you my own eye, for in it you can see the lens shining with this unnatural, because unaccustomed, light, looking like an opaque substance, a blue-green cataract, whilst my eye can hardly distinguish anything in consequence of the bluish haze which confuses my sight.

Life and death then have nothing to do with the existence of this substance; here, it is present in the living lens; it does not disappear from lenses that have been kept for months in glycerine.

I have already said that this substance not only exists in the lens, but that it can be found everywhere by treating any animal substance, first with dilute acid, then neutralizing with alkali, and then extracting with ether: thus we obtain solutions having exactly the same properties as you see in the lens. Here, for example, is such an extract from the liver. Here, from the kidney. Here, from the heart. When an acid solution of this substance is treated with ether, no fluorescent substance is obtained. First, as with quinine, the acid must be neutralized before this substance or before the quinine can be taken up by the ether.

Having then obtained these solutions, we were able to compare them with solutions of quinine in their actions on the spectrum. And first, the solution of the natural substance begins to fluoresce a little before the solution of quinine; but on carrying it on through the spectrum it ends where quinine ends.

The fluorescent light of the natural substance is a little more greenish than the fluorescent light of quinine.

If a quartz cell containing this fluid is interposed between the source of light and a solution of quinine, no fluorescence takes place in the quinine; and if quinine is interposed between the light and this natural solution, scarcely any fluorescence is observed in it.

When a solution of common salt is added to the naturally fluorescing substance, the fluorescence is almost entirely destroyed, as happens with quinine.

If the natural solution is boiled with permanganate of

potass, it does not lose its fluorescence, nor does quinine ; but when permanganate with excess of alkali acts upon this substance or upon quinine, the fluorescent substance is entirely oxidized.

Hence this substance by the mode of its extraction and by its remarkable action on light, is very closely related to quinine; and this led us to apply the chemical tests for quinine to this natural fluorescent substance, after extraction from the body.

The different tests for alkaloids like quinine, as morphia, strychnine, veratrine, atropine, you may see in the following reactions. First, quinine gives, as you see, a precipitate with iodine in iodide of potassium. Secondly, iodide of mercury in iodide of potassium also gives a precipitate. Thirdly, phosphomolybdic acid also gives a precipitate. Fourthly, bichloride of platinum gives a precipitate. Lastly, terchloride of gold causes a precipitate, and this precipitate is soluble in alcohol.

Now each and all these different reactions are obtained with these same reagents acting on the fluorescent substance that is extracted from animals.

So that here again we have chemical proof that this substance is an alkaloid, and that it is closely related to quinine.

We have named it Animal Quinoidine because we have not as yet been able to crystallize it nor to obtain enough for an analysis.

Having satisfied ourselves that an alkaline fluorescent substance resembling quinine existed in the different textures, we endeavoured to determine the proportion that was present in different parts. For this purpose standard solutions of quinine of known strength were prepared, and equal amounts of substance were treated in precisely similar ways, and then the fluorescence was compared with the standard solutions of quinine. No very accurate estimations could thus be made, but comparative results could be obtained, and these are represented in the following Tables:—

On the amount of fluorescent substance in different parts of guinea-pigs and of man, measured by the number of grains of quinine in 100 *litres* (= 176 *pints*) *of water that gave the same fluorescence.*

	In Guinea-pigs.			In Man.		
Liver	6 to 3	6	2	2	2	2
Lenses	3	2	2	2		
Kidney	3	2	2	2	2	3 to 6
Urine	3	2	2			
Bile	3	2	2			
Blood	3	2	2			
Brain	3	2	2			
Nerves	3	2	2	1	1	2
Muscles	3	2	2	1	2	2
Humours of the Eye . .	2	2	2			
Cartilages	..	..	..	3	1	
Spleen	..	..	..	1	1	3
Lungs	..	..	..	1	1	2

What, then, is the meaning of this widely diffused substance in animals which so closely resembles quinine? At present we are far from a perfectly clear answer. It is not thirty years yet since the presence of ammonia in the products of distillation of coal was considered "curious," because nitrogen was thought to be the characteristic of an animal substance, and absence of nitrogen was considered as the distinctive mark of vegetable creation. Gradually, year by year, each substance that has been thought to be the special property of the vegetable world has been found to occur in animals. Thus sugar, starch, woody fibre, vegetable colouring matter as indigo, albuminous substances, are common to animals and vegetables; and at length we have arrived at the fact that no distinction can truly be drawn between the three kingdoms of nature. In the body, salt and phosphate of lime and phosphate of soda are animal substances as much as fibrin and albumen. Sugar is as much an animal substance as albumen is a vegetable substance, and no separation can be made by chemical analysis between animal, vegetable, and mineral matter.

The processes which take place in the three different kingdoms are, however, very different. The vegetable gene-

rally from carbonic acid, ammonia, and water can synthetically build up acids, neutral hydro-carbons, fats, alkaloids, and albuminous substances. Whilst the animal generally from albumen analytically produces alkaloids, fats, neutral hydro-carbons, acids, and ultimately water, ammonia, and carbonic acid.

Thus the following table of synthetically and analytically produced substances common to both kingdoms may even now be formed:—

From Carbonate of Ammonia and Water. *Substances formed synthetically, by the plant or by the chemist.*	From Albumen passing down to Carbonate of Ammonia and Water. *Substances formed analytically.*
Oxalic Acid	Albumen
Formic ,,	Casein
Lactic ,,	Animal Quinoidine
Acetic ,,	Indican
Valerianic Acid	Glycocol
Glycerine	Taurin
Sugar	Leucin
Starch	Urea
Cellulose	Caprylic Acid
Cholesterin	Caproic ,,
Butyrin	Capric ,,
Palmitin	Olein
Stearin	Stearin
Olein	Palmitin
Capric Acid	Butyrin
Caproic ,,	Cholesterin
Caprylic ,,	Cellulose
Urea	Starch
Leucin	Sugar
Taurin	Glycerine
Glycocol	Valerianic Acid
Indican	Acetic ,,
Quinine	Lactic ,,
Casein	Formic ,,
Albumen.	Oxalic ,,

From this point of view, then, our so-called animal quinoidine is descended from albumen, and its ultimate progeny are carbonate of ammonia and water, out of which substances the cinchona tree, under favourable circumstances, is able to build up quinine $\text{C}_{20}\text{H}_{24}\text{N}_2\text{O}_2$.

From the large number of carbon atoms in quinine, it may be regarded as one of the early substances produced in the downward passage of albumen, and from this we shall very probably find the key to the question how quinine acts in the body.

When sulphate of quinine is taken, like the lithium and other substances which I brought before you last year, it rapidly passes from the blood into the textures.

Even in a quarter of an hour, after four grains of sulphate of quinine the fluorescence may rise to 75 grains to 100 litres. It is found in greatest amount in the liver and kidney; rather less in the blood, urine, and muscles; still less in the brain, nerves, and bile; and is perhaps even in this time capable of being detected in the lens of the eye.

In three hours the maximum effect of the quinine may be reached. It amounts then to from 100 to 200 grains of quinine in 100 litres of water, and it occurs to this amount in the liver, kidney, urine, bile, blood, brain, and muscles. The nerves and aqueous humour showed much less increase, and the lenses showed the least increase of all the textures.

In six hours the amount of fluorescence was rather less than in three hours.

In twenty-four hours it was considerably less than half as much as in three hours.

In forty-eight hours, except in the liver and blood, there was but little more fluorescent substance in the textures than naturally exists there.

And in seventy-two hours after the dose of quinine the liver showed no trace of increase of fluorescence.

Hence, in fifteen minutes the quinine had passed everywhere. In three hours it was at its maximum, and remained in excess for six hours. In twenty-four hours it was much diminished, and in forty-eight hours scarcely perceptible.

These results were obtained by extracting the natural fluorescent substance and the quinine together from the textures, determining the joint fluorescence by standard solutions; and by comparing the numbers thus obtained with the numbers given when no quinine was taken.

The following table of the fluorescence of the different textures after four grains of quinine had been taken by guinea-pigs was made:

	Experiment 1, ¼ hour.	Experiment 2, ½ hour.	Experiment 3, 1 hour.	Experiment 4, 3 hours.	Experiment 5, 4½ hours.
Liver . .	75	40	20 to 40	100 to 200	100
Lenses . .	6 to 3	5	..	3	2
Kidney . .	75	40	20	100 to 200	100
Urine . .	50	20 to 10	20	100 „ 200	100
Bile . .	12	20	5	100 „ 200	13
Blood . .	50	20	20	100 „ 200	12 to 25
Brain . .	12	10 to 5	5 to 3	100 „ 200	6 „ 12
Nerves . .	6	5	least	6	2
Muscles . .	50 to 25	20	5	100 to 200	50 to 100
Humours .	..	5	..	6 „ 3	2

	Experiment 6, 5½ hours.	Experiment 7, 6 hours.	Experiment 8, 8 hours.	Experiment 9, 24 hours.	Experiment 10, 32 hours.	Experiment 11, 48 hours.	Experiment 12, 72 hours.
Liver . .		100 to 200		50	4	6	6
Lenses . .		3 „ 1		3		3	3
Kidney . .		100		50		3	3
Urine . .		100	4 to 6	12 to 6	2	3	3
Bile . .		75	5	12		3	3
Blood . .	20 to 40	100 to 50		12		6	3
Brain . .		25		6			3
Nerves . .		6		3		3	3
Muscles . .		25		12 to 6		3	3
Humours .		3		6		3	least

We have been able also to find some trace of the passage of the quinine even into the lens of the eye of man.

The following table, which we owe to the kindness of Mr. Bowman, who gave us the cataracts, makes this evident:—

On the increase of fluorescence in cataracts after quinine.

Natural fluorescence of the lens	=	1·6 grs. of quinine per 100 litres of water.		
1 hour after 5 grs. quinine; cataract	=	1·6	„	„
1¼ „ „ „	=	1·6	„	„

2 hours after 5 grs. quinine; cataract	=	1·6 grs. of quinine	per 100 litres of water.
$2\frac{1}{4}$ " " "	=	2·1 to 3·1 "	"
After many days taking quinine "	=	6·2 to 3·1 "	"

The figures represent the number of grains of sulphate of quinine in 100 litres, 176 pints of water, required to give a fluorescence equal to that of the substances extracted.

Thus, then, the quinine goes everywhere; and wherever it goes it meets with the natural fluorescent substance like quinine which most probably is constantly forming and undergoing oxidation. The incoming quinine causes a temporary excess of quinine in the textures. Probably it causes a stoppage of the fresh formation of quinine from albumen; a temporary arrest of the changes going on; a transfer of action perhaps to the quinine introduced, so that with large doses deafness and great prostration and almost imperceptible pulse are produced in man, whilst in guinea-pigs death even is caused by the extreme prostration. In small doses, quinine, probably like alcohol, gives an immediate stimulus when the first chemical action takes place; but soon the quinine retards the chemical changes in the nitrogenous substances, just as alcohol, by its secondary action, retards the chemical changes in the hydro-carbons in the different textures.

Possibly the increased resistance to changes in the textures and in the blood produced by excessive doses of quinine or alcohol corresponds to that state well known to medical men under the very indefinite and very often incorrect name of uremia.

From these experiments two hopeful prospects of possible discovery arise—1st, as to the explanation of the cause and cure of ague; 2nd, as to the treatment of diseases in parts of the body external to the blood vessels.

1. Assume that a substance like quinine exists, in health, in the textures, can its rapid destruction and removal through the action of marsh miasm give rise to ague? Does quinine cure ague by furnishing a substance which retards the changes which go on in the textures? and in the well-known property of arsenic to preserve organic substances have we also the explanation of its power in curing ague?

2. If the chemical circulation can carry alkaloids even into the non-vascular tissues, is it not reasonable to suppose that medicines pass outside the blood and act on the textures? and is it not most probable that they take part in every chemical change that occurs outside the blood-vessels, as well as within the blood itself? Still further, may we not expect that among the multitude of new substances which synthetical chemistry is now constantly forming, some medicines may be discovered which may not only have power to control the excessive chemical changes of the textures in fevers and inflammations, but may be able to remove the products of insufficient chemical action even in those diseases which affect the non-vascular textures, as, for example, in cataract and in gout?

It remains that I should in a very few words tell you what was already known regarding this fluorescent substance, and on the rate of passage of alkaloids into and out of the body, before we began our work.

In 1845, Professor Brücke stated that the lens absorbed the blue rays of light to a very great extent, and that the cornea and aqueous humour did so to a less extent.

In 1855, Professor Helmholtz examined for fluorescence the retina of the eye of a man who had been dead for eighteen hours. The first experiment showed that it was very feebly fluorescent. The colour of the light dispersed through the retina he found greenish-white.

In 1858, M. Jules Regnauld, using sun-light, found in man and the mammifera that the cornea fluoresced in a very slight degree. In the sheep, dog, cat, and rabbit the crystalline lens possessed in the highest degree fluorescent properties. In these animals, and also in many birds, the central part of the lens, preserved by desiccation at a low temperature, retained this property. The central portion of the crystalline of many aquatic vertebrata and mollusca he found almost entirely without fluorescence. The vitreous humour possesses only a very feeble fluorescence, due to the hyaline membrane. The retina possessed a certain fluorescence which was not at all comparable in intensity to that of the crystalline lens.

In 1859, I. Setschenow, of Moscow, a pupil of Helmholtz,

at his request, experimented on the eyes of men and rabbits. The fresh retina showed the same phenomenon as the dead human retina. It diffused a greenish-white light, which, examined by a prism, gives a spectrum in which the red is wanting. The vitreous humour in a thin glass vessel showed only traces of fluorescence. The lens, on the contrary, fluoresced very strongly, the colour of the dispersed light being white-blue, exactly like quinine, only the quinine was a little stronger. Examined by a prism, the dispersed light gave a spectrum in which the red was wanting, and in which the blue tone predominated. The fluorescence he found begins as in quinine solutions between G and H, and is strongest at the outer edge of the violet rays, and extends into the ultra violet to the same distance in the case of the lens as in the case of a quinine solution. When the cornea was cut out, it fluoresced much feebler than the lens; the aqueous humour did not fluoresce at all.

The appearances in the three last media, he says, can be shown with the greatest ease, even in the eye of the living man. When the eye is brought into the focus of the ultra violet rays immediately the cornea and the lens begin to glimmer with a white-blue light. The cornea in the living eye is much more fluorescent than when dissected out, probably from the loss of transparency, consequent on contraction of the texture, and from evaporation.

With regard to the rate of action of alkaloids; Professor Donders has carefully investigated the time in which atropine and Calabar bean act on the iris in man.

A solution of atropine dropped on to the cornea in 15 minutes begins to act, and attains its maximum action in from 20 to 25 minutes. In 42 hours the pupil is rather smaller, and even after 13 days the pupil was not quite its natural size. The fluid extracted from the aqueous humour, injected into another eye, caused dilatation of the pupil.

A solution of Calabar bean began to act in from 5 to 10 minutes; attained its maximum action in from 30 to 40 minutes. At the end of three hours it began to diminish, and the effect disappeared entirely in from two to four days.

LECTURE III.

DIABETES.

I HAVE chosen diabetes for my third lecture, because, among all the diseases to which mankind is liable, it is the best example of a purely chemical derangement of health.

In slight, or in severe cases, even from first to last, mechanical symptoms or complications rarely occur. Loss of nutrition and loss of power through the whole course of the disease bear a direct relation to the loss of saccharine fuel, and when the complaint proves fatal, no change of structure is found; no evidence of any disordered chemical action remains. Atrophy alone shows that the nutrition of the body has become more and more feeble.

Throughout its course the disease seems as though it might be cured at any moment, provided some change could be made in the chemical actions on which the production of the sugar depends.

There appears to be only one link wanting to make the healthy chain of action complete; if this could be supplied the disease would cease to exist; the sugar would disappear from the urine, and the symptoms of the complaint would be gone. What, then, is the nature of the disease? To understand it I must go back to physiological chemistry.

Very many substances are included in the term sugar. Though closely related, they have chemical and optical differences. The three great optical divisions of sugars are—1. Convertible, polarizing to the right—these are cane sugars. 2. Inverted, polarizing to the left—these are fruit sugars. And, 3. Unconvertible, polarizing to the right—these are glucose and diabetic sugars. The chemical differences are best seen in the following table:—

Crystallized cane sugar	$C_{12}H_{22}O_{11}$
Combined cane sugar	$C_{12}H_{18}O_{9}$
Grape sugar, crystallized	$C_{12}H_{28}O_{14}$
Grape sugar, in combination	$C_{12}H_{22}O_{11}$
Melitose, from Eucalyptus mannifera	$C_{12}H_{24}O_{12}$
Eucalyne	$C_{12}H_{24}O_{12}$
Melezitose	$C_{12}H_{22}O_{11}$
Sorbin	$C_{3}H_{6}O_{3}$
Sugar from secale cornutum, mycose	$C_{12}H_{26}O_{23}$
Caramel	$C_{12}H_{18}O_{9}$
Mannite	$C_{6}H_{14}O_{6}$
Dulcose	$C_{16}H_{14}O_{6}$
Erythromannite	$C_{4}H_{10}O_{4}$
Pinite	$C_{12}H_{24}O_{10}$
Quercite	$C_{12}H_{24}O_{10}$

In addition to these there are saccharine substances of animal origin, of which the best known are—

Milk sugar, crystallized	$C_{12}H_{24}O_{12}$	
Milk sugar, in combination	$C_{12}H_{20}O_{9}$	
Glycogen	$C_{12}H_{20}O_{10}$	Bernard's saccharine substance from the liver.
Inosite	$C_{12}H_{24}O_{12}$	Scherer's sugar from the heart and other muscles.

All these different saccharine substances are not able to pass as glucose into the urine; but they are all capable of being oxidized in the blood and textures into carbonic acid and water, whilst giving heat or motion, or other energy, to the body.

Each grain of starch that is taken as food, when acted on by the saliva or pancreatic fluid, is converted into sugar, and becomes a source of fuel or power, and ultimately passes out of the body as carbonic acid and water.

In diabetes the starch is still changed into sugar; but in the circulation and in the extravascular or parenchymatous structures the further change is partly or wholly stopped; more or less of the sugar remains as sugar, part reaches the kidneys and is thrown out in the urine, part exists in the structures unchanged; and thus the system is deprived of one part of that conversion of latent into active force on which the nutrition and power of the organs depends.

In the body or out of the body, when once a series of chemical actions is set up, the series tends to become continuous; it propagates itself, unless a change of conditions occurs.

For example, grape juice will remain as grape juice, if kept from the action of other substances. Under well-known conditions it will ferment, and continue fermenting, as long as sugar, and ferment, and the proper temperature are present. If the conditions are slightly varied, variations in the products will be observed. The series of actions will not pass rapidly from grape juice to alcohol, to vinegar, or to putrefaction; but according to the conditions one action or another action will be set up and will continue as long as that action is possible.

In health and in diabetes the sugar is subjected to different conditions. In health the chemical changes are propagated and continued to their full extent; whilst in diabetes the conditions necessary for perfect change are wholly or partly wanting. These conditions, on which the changes depend, are chiefly three. 1st. The proper temperature; 2nd. The presence of a not immoderate quantity of sugar; 3rd. The presence and activity of the proper ferment.

On each of these conditions a few words are necessary.

First, the internal temperature of the body, under all circumstances, is subject to so small a variation, that at present there is no proof that such a reduction can occur as can check the chemical actions in the human body, though under certain circumstances small animals can be exposed to cold so that sugar may be made to appear in the urine.—*Proceedings of the Royal Society, December* 15, 1864.

Secondly, by the most careful investigation, I have satisfied myself that Professor Brücke is right in saying that healthy urine contains sugar—that is, the amount of sugar derived from the food, or from the changes going on in the textures, is at all times more than can be entirely changed in the circulation and in the tissues. If, then, a considerable amount more is thrown into the circulation, some of it will pass out in the urine. Thus an injection of sugar into the rectum when absorbed causes temporary diabetes; so, also, large quantities of sugar, fruit, and farinaceous food tend to produce temporary diabetes. Thus, also, if Bernard's amyloid or glycogenic substance is produced in excess in the liver, diabetes is the result.

Thirdly, the ferment, the prime cause of change, has not been yet insulated. Whether it be the albuminous substance of the saliva or pancreatic fluid, or some other of the many albuminous substances in the blood, it requires for its action heat, the presence of alkali, and an undisturbed circulation of the changing fluid.

With regard to the effect of alkalies, something will be said when I speak of the treatment of diabetes; but concerning the influence of unobstructed chemical action some remarkable physiological experiments must be here mentioned, because they not only furnish the most striking illustrations of the relations of mechanical to chemical disease, but because they also help to account for the effect of sudden mental shocks and nervous disturbances, which do so much harm to diabetic patients.

Bernard made the great discovery that the mechanical injury of the floor of the fourth ventricle of the rabbit alters the chemical actions going on in the body so as to cause sugar in excess to appear in the urine. This is a most remarkable demonstration of the relation which subsists between mechanical and chemical actions in the living body.

M. Schiff, in his 'Untersuchung uber Zuckerbildung' (1859), states that this diabetes results from injury of the vaso-motor nerves of the abdominal organs which arise from the thalami optici and the crura cerebri—*partent des couches optique et des pedoncules cérébraux;* and he also shows that by injury of other parts of the nervous system temporary or permanent diabetes may be produced.

Thus cutting the posterior roots of the nerves arising from the cervical portion of the cord, leaving the anterior roots untouched, causes temporary appearance of sugar (irritative diabetes); whilst by division of the anterior roots on a level with or above the fourth cervical vertebra, permanent (or paralytic) diabetes results. These injuries, he says, cause an irritation or a paralysis of the vaso-motor nerves. The vessels of the liver become dilated and distended; and as a consequence there is an excessive secretion of glycogen by the liver.

The permanent diabetes may be thus occasioned; but it is

far more probable that the temporary diabetes is owing to the mechanical injury of the nervous system so affecting the vessels that the chemical changes are interrupted. The same phenomenon is seen in every fermentation. The chemical action is temporarily stopped when the fermenting fluid is disturbed by any sudden change.

These conditions of change may in diabetes be affected singly or all simultaneously. When the affection reaches to the extent of stopping the chemical change in the vegetable or animal sugar in the body, diabetes, intermittent or permanent, is the result.

That the disease is only a little way distant from health is shown by the existence of sugar in the urine in the healthy state; so that a small quantity of sugar in the urine is no proof of disease; and here, as elsewhere, there is no defined limit where health ends and disease begins.

Diabetes is the arrest of a healthy state; an increased quantity of sugar appearing in the urine, because the actions that constitute health are lowered.

In perhaps half the cases of diabetes the arrest of change in the food-sugar constitutes the complaint. This is proved by the fact that when a strict antifarinaceous diet is observed the abnormal amount of sugar ceases, and the patient is well as long as he keeps to the strict diet. When this fact was published in 1806 by Dupuytren and Thenard, they used these words:—"Que le traitment qui consiste surtout dans un régime purement animal a le même degré d'efficacité que le quinquina dans les fièvres intermittants."—*Annales de Chemie*, vol. lix., p. 45.

But it was soon found that cases occurred in which a strictly antifarinaceous diet, consisting of animal food and water, did not stop the sugar in the urine. For days and weeks not a grain of vegetable starch or sugar may be taken as food, and yet sugar in excess will exist in the urine. Whence does this sugar come? It must either be taken in the animal food or it must be produced in the body.

Previous to Bernard's discoveries, this production of sugar when no vegetable food was taken admitted of no explanation.

Now, the discovery of the amyloid substance in the liver, and of inosite in the muscles, lungs, brain, and other organs, gives a full solution of the difficulty. In the chemical changes going on in the body, animal starch is formed in the liver, and in other organs, as in the prostate gland, and sugar in the muscles; not, as in vegetables, by the fixation of carbon and the decomposition of water by the action of light, but more probably by the gradual splitting up of the higher organic compounds of the different organs whilst performing their functions.

The good effect of an antifarinaceous diet in some cases, and its want of effect in others, marks the two great divisions of the disease—the two stages of diabetes. In the first stage vegetable sugar alone ceases to go through the healthy chemical changes, whilst the animal sugar is entirely changed; in the second stage, animal sugar as well as vegetable sugar are more or less unchanged. It may be concluded that animal sugar is more readily changed than vegetable sugar; and when in diabetes an antifarinaceous diet has no marked effect, then the conditions of change of the sugar in the body are furthest from the healthy state.

There is sufficient evidence that diabetes does not always progress from one stage to the other. The disease may halt anywhere in its progress, and remain stationary for years, or get better or worse. A gentleman has consulted me for the last four years occasionally; he is now 57. When I last saw him the specific gravity of the urine was 1020, about three pints in twenty-four hours, containing about four grains of sugar to the ounce. He had been diabetic for twenty-nine years, during which time he married, and has now healthy children grown up. When he takes care about his diet, the sugar and symptoms vanish, but when careless, the symptoms return, and the sugar can be found in the urine.

Diabetes, then, in its mildest or first form, is the loss of power to change the sugar of the food; in its more advanced or more intense form, it is the loss of power to change the sugar produced in the organs and textures of the body, as well as in the food. The chemical changes in the animal as well as vegetable sugar are more or less arrested.

On the Means of Detecting Diabetes.

The first and readiest means of detecting diabetes is to boil about a drachm of urine and a drachm of liq. potassæ for two or three minutes in a long test-tube. The colour of the urine after boiling should be compared with an equal quantity of urine mixed with as much water in another test-tube. In well-marked cases the boiled urine becomes darker than the darkest sherry. If the colour is only slightly changed, then the same quantity of urine should be mixed with two drops of a saturated solution of sulphate of copper and a drachm or more of liq. potassæ, and then boiled. Reduction of the copper rapidly takes place if much sugar is present; or half-an-ounce of urine should be boiled with ten grains of slaked lime. If none of these tests give a decided reaction, the amount of sugar in the urine may be considered scarcely beyond the quantity that exists in health. Before asserting that no tendency to the disease is present, it is well to repeat these tests with urine made about two or three hours after a farinaceous meal.

A gentleman was sent to me from the country for diabetes. His medical man had found the sugar, and had put him on an antifarinaceous diet. When he came to me the colouration and reduction, on testing the urine, were not perceptible. A portion of this urine was sent back with the patient, and the medical man was surprised to find that the sugar was gone. When the patient returned to farinaceous diet the sugar re-appeared in the urine.

On the Difficulties and Fallacies of the Tests for Sugar.

Regarding the presence or absence of very small quantities of sugar, positive and negative doubts may arise. Appearances may be observed resembling sugar when no sugar is present, and substances may hinder the reactions taking place when sugar exists.

When there is more than a grain of sugar in the ounce of urine, little difficulty occurs in finding it. When less is

present, the organic matters in the urine hinder the reactions, and it becomes necessary to separate the sugar from other substances before the tests are used.

In a paper in the 'Quarterly Journal of the Chemical Society,' vol. xiv., p. 27, "On the Detection of Sugar in Healthy Urine," you will find experiments on the value of the different processes for determining the presence and quantity of small quantities of sugar in the urine. In doubtful cases, by following Brücke's process, no case of diabetes can be overlooked.

There remains, then, the opposite error that may arise from the use of the sugar tests. Sugar may be thought to be present when the colouration or reduction may be caused by some other substance than sugar, as uric acid.

Long-continued boiling of the urine, even without alkali, causes the colour to become darker. The longer the boiling is continued the darker the colour becomes. Alkalies and heat together always have some darkening effect on the healthy colouring matter of the urine when exposed to the air.

When accidental colouring matters are present—as, for example, rhubarb or senna—alkali, without heat, gives a deep colour to the urine.

On this account, the test of colouration ought never to be trusted to alone. Reduction of the oxide of copper must occur if sugar is present; but substances may coexist with the sugar, as muriate of ammonia, 1 grain to $\frac{1}{200}$th grain sugar; or urea in great excess, 1 gr. urea $\frac{1}{1000}$th gr. sugar; and these substances may hinder the reduction of the copper; or substances may be present when no abnormal sugar is in the urine, which may reduce the oxide of copper and lead to great errors.

In the Medico-Chirurgical 'Transactions' for 1843, vol. xxvi., p. 211, in a paper on the detection of sugar in diabetic blood, I mention that uric acid will reduce the oxide of copper.

Tartaric acid also, under certain circumstances, will reduce the oxide of copper.

A physician sent me some urine of a supposed diabetic patient, asking me to determine the amount of sugar. I told

him I found no sugar present. He gave me an analysis in which the sugar was determined to the second decimal place. I took the urine I had examined to the analyst, and asked him to repeat his test. For convenience he had made a Winchester quart of Fehling's standard solution, and on testing the urine, reduction occurred to an immense extent; and the analyst thought I was wrong, until I heated his standard solution without adding any urine to it. Then the tartaric acid reduced the oxide of copper just as if sugar had been present.

These examples, and more might be given, of the reducing action of other substances than sugar are quite sufficient to show that no dependence can be placed on the reduction test alone. It would be just as wrong to assert that all reduction proves the presence of uric acid, as to say that it alone indicates sugar.

On the Quantitative Tests for Sugar.

A practised eye can make an approximation to the amount of sugar by the colour produced by potass or lime, as a practised hand can tell nearly the weight contained in it; but thus no accurate results can be obtained.

The quickest and easiest method is to fix the amount of sugar by Soleil's saccharometer. The decoloration by animal charcoal or acetate of lead causes a loss of sugar, because a portion is always retained with the colouring matter (see 'Quarterly Journal of Chemical Society,' vol. xiv., p. 28); but by using as little decoloriser as possible, this instrument gives accurate results; whilst for rapidity, and ease, and beauty, it far surpasses any other process.

Fehling's standard copper solution is easily, quickly, and accurately useful. I have already shown the necessity for testing the test.

The fermentation test requires considerable care, much time, and a good balance. At page 27, vol. xiv., of the 'Quarterly Journal of the Chemical Society,' you will find a comparison of these different processes.

Lastly, the specific gravity has by some persons been used

as a means of determining the amount of sugar in diabetic urine.

Formulæ are given in books for calculating the sugar from the gravity of the urine. These tables might give a good approximation to the truth if diabetic urine were a solution of sugar in distilled water; but there are very many other substances present with the sugar, and these all vary as well as the sugar, and they all affect the gravity of the urine, and render all the formulæ worthless. To convince you of this I have made the following table from ten cases of diabetes. The amount of sugar present in an ounce of urine was determined by the saccharimeter. The specific gravity was determined by a first-rate balance.

Sugar to the ounce of urine. Grains.	Specific gravity.	Sugar to the ounce of urine. Grains.	Specific gravity.
1	1030·8, 1029·5	18	1048·6
2	1009·2, 1025·6, 1031·2	19	1031, 1037·8
4	1028·5, 1029·6	20	1033·0, 1037·8, 1039·0, 1042
5	1013·8, 1014·4, 1027·8, 1029·6	21	1032·8
6	1034·4	23	1033·4
7	1029·4, 1033, 1035·4	24	1032·0, 1035·0, 1035·4, 1036·8, 1043·4, 1044·4, 1045·4
8	1027·3	25	1030·0, 1033·9, 1044·8, 1045·8
10	1029·2, 1031·0	26	1034·6, 1037·8
12	1024·5	27	1037·6
13	1033·4, 1043·4, 1045·0, 1045·4, 1045·4	29	1041·2
14	1023·2	30	1035·4, 1040, 1042
15	1028·5, 1030·1	33	1033·4, 1040·5
16	1032·4, 1034·0, 1034·8, 1035·0	34	1044·0
17	1025·6, 1030·2, 1035·4	37	1039·4, 1043·4

The want of any correspondence between the amount of sugar and the specific gravity is very striking. Thus, 13 grs. to the ounce have a higher specific gravity than 37 grs. to the ounce. Twenty-four grains to the ounce in six different specimens give widely different specific gravities, proving that

no dependence must be placed on any tables for calculating the sugar.

Or the following table from the urine of a single patient, aged 21. The analyses were made between February and November, by Mr. Kemp, of Edinburgh :—

Specific gravity.	Quantity of Sugar per ounce urine. Grains.	Specific gravity.	Quantity of Sugar per ounce urine. Grains.
1023	2·2	1031	14·5
1025	2·1	1032	17·5
1026	4·0	1033	6·0
1027	0·7 4·5 4·5	1034	8·0
1028	14·5	1035	10·0
1029	3·3 2·5 3·	1036	5·5
1030	3·6 7·2	1038	7·5

Here is another case, with greater variations in the specific gravity. The sugar was determined by the saccharometer :—

Specific gravity.	Quantity of Sugar per ounce urine. Grains.	Specific gravity.	Quantity of Sugar per ounce urine. Grains.
1013·8	5	1034·0	16
1014·4	5	1035·4	7 17
1023·2	14	1037·5	19 20
1025·6	2	1038·3	3
1028·5	4	1039·0	20
1029·6	4	1043·4	13
1030·0	15	1044·4	24
1031·0	10	1044·8	25
1031·2	2	1045·0	13
1032·2	24	1045·4	13
1032·4	16	1045·8	25
1033·4	13	1048·6	18

What are the Symptoms of the Disease?

In slight cases there are literally no symptoms at all. In the 'Medico-Chirurgical Transactions,' vol. xxxvi., p. 424, you will find this case: A gentleman, aged 63, in 1847 consulted Dr. Watson, who wrote me this note. "He calls himself well, and seems eminently so. Stout, fat, and ruddy; eats and drinks heartily and indiscriminately, and has no dyspepsia.

Perspires copiously. Makes much urine, and often by day and by night, and has done so these forty years. Says his pulse occasionally intermits, and has long done so. I found it steady and at 80 in the minute. His father died of diseased heart at 77. My patient had some bronchial trouble last winter. Had lately some redness of the toe for a day or two. Comes to me that I may see what he is when well, as he means to put himself under my charge whenever he is ill." He had noticed some floating substance (not sand) in his urine, and was curious to know what it might be. I found the urine had specific gravity 1032·0, and it contained slight but decided evidence of sugar. In a year and a-half another examination found more sugar, and four years after that I found three grains, and on another occasion five grains of sugar to the ounce. There were no other symptoms of diabetes.

Usually the sugar acts as a diuretic and causes thirst, whilst the appetite is often voracious; but although much is eaten, the strength and flesh more or less rapidly fall off.

A girl, aged 18, was in St. George's Hospital April, 1852, who said she ate a two-pound loaf at each meal, and that she drank a pail and a half of water daily, and rapidly grew thin and weak. After her admission she passed twelve pints of urine in twenty-four hours.

A labourer, aged 32, when admitted, told me his water ebbed and flowed. The greatest flow, he said, was seven gallons, the ebb five pints.

With regard to the loss of flesh take the following statements :—

A gentleman, aged 62, at the beginning of the disease lost two stone in three months.

Another, aged 37, in August, 1852, lost fourteen pounds in five days, passing two gallons of urine, sp. gr. 1050, daily.

A physician, aged 72, told me that in four or five months he had lost forty pounds weight, but he regained most of his loss.

The following is the best example I can give you of the symptoms in an acute case :—

On the 15th of September, 1852, I was requested to see a gentleman, about 35 years of age, who six weeks previously was quite well, and shooting in Scotland, where he drank freely of whiskey and took excessive exercise. He at that time passed a considerable quantity of urine, which he attributed to the whiskey, and yet he was advised to consult me when he returned to London; so that he must have had some doubts about the cause of the excessive secretion.

When he came back he was depressed, and had great trouble with his bowels. He stayed from his occupation for some days, but returned to it, thinking he was getting better, when he was attacked by great constipation of the bowels, much weakness, dry tongue, and soreness of the throat.

I then saw him, in bed: he could at first hardly speak, from apparently nervous anxiety and dryness of the mouth. There was no soreness of the throat to be seen. The tongue was quite clean. The pulse 110, and very feeble. The skin harsh and dry. He was not very much emaciated. The urine was clear, not above two pints. He had had a very confined motion, which he said burnt his inside in passing. He had a very unquiet night. The pupils were natural. The head quite clear, and after some time he spoke in a good voice, and complained only of weakness. I examined the lungs and heart, and they were quite healthy. I could find nothing wrong with the abdomen: it was rather hard and retracted. He did not complain of thirst, and could eat nothing. I had some trouble to persuade him he was far more anxious about himself than he ought to be, and that he was doing himself harm by it. I urged him to take jelly and brandy, and said that I would see him again after I had examined the urine.

On my way home I remarked to his medical man that possibly it was a case of acute diabetes, and that if so it was a bad case.

On examining the urine it had specific gravity 1030, and contained sugar.

The following morning I went to his medical man to say

it was diabetes: he said, "I was coming to you to tell you that he is dying."

I saw him at half-past twelve on the 16th of September, perfectly comatose, and we tried in vain turpentine injections and blistering with ammonia. He died in about an hour.

The prognosis in diabetes depends chiefly on the nature of the attack, and on the constitution and age of the patient.

It is very difficult to decide upon the severity of an attack, because the disease does not usually proceed at a uniform rate. At one time the chemical change of the vegetable and animal sugar seems almost entirely stopped. Sugar, thirst, thinness, and weakness increase rapidly. After a time a reaction may occur. The sugar may almost or altogether disappear from the urine. The symptoms may pass away, and some part or all of the flesh and strength lost may be regained. Anywhere in the course of the complaint such a halt may occur, and the disease may stop for months or years. In some rare cases even the worst possible diet appears not to affect the progress of the complaint. Sufficient chemical change goes on to supply the heat and the force of the body, and sufficient nutrition takes place to keep the organs healthy. In this condition scarcely any exertion of physical or mental power is possible. It is sufficient work to live, but with care life may so last for years.

The increase of urine, of debility, and of emaciation in any fixed period may be taken as indices of the severity of the attack during that time, but not at any other, for the disease may become more or less severe; so that the future cannot be surely known from the past.

The goodness or badness of the constitution as regards diabetes usually may be estimated by the family disposition and by the weight of the patient. That a mode of chemical action should be propagated from parent to child, or that many children of the same family should lose the power of changing sugar into carbonic acid and water are examples of the law that like begets like. This law is so universal that in this instance as in other instances it is apt to be used as a solution when it is only a cloak for a difficulty. The trans-

mission of peculiar features, habits, and dispositions is just as inexplicable as the inheritance of imperfect chemical change of sugar in the human body.

A shoemaker, aged 51, was in St. George's Hospital, having suffered from diabetes for four years. He had two daughters, one 12, the other 5. The eldest was healthy; the youngest was admitted with diabetes, having been ill about six months. She died before her father.

I was asked about a suspected diabetes in a boy whose sister had died when she was 7 years old, after being ill two years with diabetes. Another sister died of the disease when 4½ years old, after one year's illness; and a brother died when 15, after three years' illness. Post-mortem examination showed no tubercular disease in any of the three children.

If, then, there is a family history of diabetes, the constitutional worth of the patient may be estimated by inquiring into the intensity of the disease in other members of the family; for sometimes only a very slight disposition to diabetes is inherited.

I have attended three brothers, all clergymen, the eldest died aged 74; the second is now 68, and the youngest is a year or two younger. All of them have had intermittent attacks of diabetes. In the eldest I found sugar in the urine thirteen years before his death. In the second, sugar was found by Dr. Prout sixteen years ago, and he is now in good health, with sugar occasionally, not constantly, in the urine. In the youngest I found sugar eight or nine years ago, and he is now, I believe, in good health. This instance shows that occasionally the inherited disposition may induce only a very slight form of diabetes. Great accumulation of fat is also an inheritance in some respects allied to diabetes. Obesity may depend on an arrest of oxidation of fatty matter, and Dr. Prout long since remarked the tendency of fat people to diabetes. The increased liability is compensated by the mildness of the attack. The store of oleaginous fuel seems to counteract the waste, and sustain the force of the body, and the greater the accumulation of fat, the less the loss of the

saccharine food appears to be felt. On the contrary, very thin people, having no supply of oleaginous food in reserve, are unable long to endure the continuous loss of the saccharine fuel, on which the force of the mainspring of the body partly depends.

If, then, the patient is fat and the family history is good, the constitution may be considered most fitted to resist or to recover from an attack of diabetes.

Lastly, in the prognosis, the age of the patient must be taken into account. In the eighteenth volume of the 'Medico-Chirurgical Transactions,' page 421, I have stated that in twenty-nine cases of diabetes eleven were above 60, and six above 70; and of these eleven all but one had the disease so slightly that it could hardly be known by the general symptoms. The diabetes of old age is rarely severe, but exceptions do occur, and at page 428 I have given a case in St. George's, aged 74: thirteen pints of water in twenty-four hours were passed, and in four months the disease was fatal.

The age of the youngest diabetic patient I have known was three years and a-half. The specific gravity of the urine was 1037. No sugar was in the urine on October 31, but it was found on December 14. The patient lived not quite one year. The sister was five years old when the sugar was first found. The highest specific gravity of the urine was 1043. She lived twenty months.

Hence, a very thin and very young child, in whose family severe diabetes is known, who is rapidly losing strength and weight, passing much water, is the worst possible case of diabetes; whilst an old, stout man, in whose family no diabetes, or very slight diabetes, is known, who loses no strength or weight, and passes but little more than two pints of water, may almost be considered as having no disease at all.

On the Complications that occur in Diabetes.

There is no special complication belonging to diabetes, unless it be cataract. Generally it may be said that all the

accidents of the disease are not owing to the diabetes, but to the debility which that diabetes produces. Thus, imperfect nutrition of the skin occurs, as in eczema, lepra, boils, carbuncles, mortification; or imperfect nutrition of the mucous membrane, as in irritations of all the mucous surfaces; or imperfect nutrition in the basement membranes or parenchyma of organs, as in phthisis.

Usually diabetic patients are exempt, in consequence of the low state of oxidation, from acute inflammations, and from stone and dropsy, on account of the diuretic action of the sugar.

The experiments of Drs. Kunde, Mitchell, and Richardson on the production of cataract artificially by loading the blood with sugar furnish the most perfect demonstration of the fact that a chemical condition of the blood is capable sometimes of producing a mechanical alteration of the structure of the lens. In the early part of this lecture I dwelt on the reverse relation of chemical to mechanical disease—that is, on the injuries of the nervous system causing diabetes, and in this formation of cataract we have diabetes producing a mechanical complaint; and this complication occurs in nature so frequently that the connection has been observed by many physicians.

Although only one direct complication of diabetes exists, yet the debility induced by the saccharine diathesis gives rise to many other diseases. It must, however, be remembered that debility arising from any other cause will give rise to exactly the same complaints.

The following remarkable cases will bring before you one of the frequent terminations of diabetes. A young lady, aged 19, passing four quarts of urine, specific gravity 1048, had probably been diabetic for twelve months. She gradually was growing weaker, when a sudden prostration of strength took place. After stertorous breathing for three hours, she became conscious, remained so for ten or twelve hours, again became comatose, and in twelve more hours she died.

A man, aged 36, came to me from Reading. He passed eight or ten pints of urine, specific gravity 1030, containing twenty-five grains of sugar to the ounce. He spoke of being

able to walk two miles. On his return the same day from London, he passed a very restless night, and in the morning his breath was hurried; his pulse very quick and very weak. There was great inclination to stupor, though when aroused he was quite clear. He gradually became comatose, and died in thirty-six hours from his return home.

A gentleman came from Vichy in a very debilitated state. He had been three years under my care. His appetite was very small, and his emaciation and weakness very great. By great quiet he was regaining strength, when he was suddenly seized with nausea, and vomited once in the evening. He passed a very restless night, with retching and extreme debility. I went early in the morning to him, and found him comatose; and within twenty-four hours of the first sickness he died insensible.

A young lady, aged 15, with urine specific gravity 1055, came eighty miles for advice, and returned the day after. "The journey prostrated her to the most frightful degree." "She was unable to help herself in the least." During this extreme illness the diabetic symptoms disappeared. By no test could sugar be found. After a few days of the greatest danger, she gradually improved; the urine became five pints in twenty-four hours, sp. gr. 1041. Six months afterwards the specific gravity was 1022. Sugar was present, but the general symptoms of the complaint were better.

In other weakening diseases the same attacks of prostration occur, and are often fatal. I went into the country to see a gentleman, about 45, who for some years had been my patient with dyspepsia and wasting; and perhaps latterly he may have had miliary tubercles in the lungs. I found him drinking port wine after dinner; hardly able with help to put on his coat when I had taken it off to examine his lungs. He was fearfully emaciated, but able to walk a few minutes in the air daily. Seeing his weakness, I examined him with the least possible fatigue. A few hours after I left him he complained of excessive feeling of debility. He gradually became comatose, and died in twelve hours after my visit.

Almost every month, at St. George's Hospital, during my

admission week, I was able to trace the fatal effect of even very short journeys in very low states of different diseases.

The next consequence of extreme debility produced by diabetes that must be noticed is the deposit of tubercles. Phthisis has been considered as one of the necessary results of diabetes, but this is very far from the truth. When the nutrition of the body is feeble, tubercles are always ready to form, and every cause of feeble nutrition, including diabetes, produces a tendency to tubercular disease. Thus phthisis is not a secondary, but a tertiary result of diabetes. The imperfect nutrition produced by the sugar in the blood and extravascular tissues is the root of the evil. Among the rich, who can afford every strengthening food, phthisis is comparatively a rare ending of diabetes. Still, it occurs sufficiently often to prove how helpless medicine is to promote the nutrition of the body when the nutriment itself becomes loaded with matter which hinders healthy action from taking place.

Another consequence of the feeble nutrition of the body is degeneration of the kidneys. Bright's disease may doubtless precede diabetes, although I have never seen this sequence. The reverse very frequently occurs; in the progress of the diabetes at varying times traces of albumen may be found, and gradually with great fluctuations the albumen increases, and ultimately the two complaints modify one another, so that I am accustomed to think sometimes that it is better to have these two diseases together than either of them separately. The increased flow of urine produced by the diuretic action of the sugar compensates for the imperfect filtration effected by the diseased cortical structure of the kidneys; and for years I have watched the diabetes stationary or lessening, or occasionally disappearing, whilst the Bright's disease slowly increased and caused its secondary or tertiary symptoms, which gradually destroyed the patient.

On the Treatment of Diabetes.

Almost every substance in every Pharmacopœia has been tried as a specific for diabetes; but hitherto no remedy has

been found to have a constant effect in stopping the sugar from appearing in the urine.

This by no means renders it impossible or improbable that some substance may be discovered which may be able to effect a perfect cure of this functional disorder.

Meanwhile the effect of diet is far beyond that of any known remedy.

An antifarinaceous, or, in other words, an antisaccharine diet will remove the sugar from the urine, and stop all the symptoms of the complaint in all those cases in which the power of consuming the animal sugar remains unaffected.

Even when the consumption of the animal sugar is imperfect or impossible, an antisaccharine diet will lessen the thirst, the flow of water, the dryness of the mouth, and even the constipation, and check, though it may not stop, the waste.

The simplest formula for the diet may be thus stated. All animal produce, including fish, flesh, fowl, game, eggs, cream, and meat soup should be taken; and all vegetable food that contains starch, dextrin, and sugar should be avoided.

As generally it is of the utmost importance to shun the forbidden food, I shall dwell upon it first.

The vegetable substances that contain most starch, dextrin, and sugar are rice, maize, arrowroot, sago, potatoes, oatmeal, peas, beans, bread, biscuit, toast, maccaroni, vermicelli, and all confectionery.

Fruits are even worse than vegetables. Apricots, plums, peaches, cherries, pears, gooseberries, are nearly as bad, and some worse, than rice or maize. Stout, porter, and ale, cider, port, madeira, champagne, and sherry are more or less highly saccharine; cocoa and chocolate contain near 20 per cent. of starch and dextrin naturally, and more is often added.

The harm of each of these substances may be determined by the amount of starch, dextrin, and sugar they contain.

The following table, in which the fruits and farinaceous vegetables are taken as perfectly dry, will answer many questions regarding the diet of a diabetic patient:—

	Amount of Starch, Dextrin, or Sugar.
Ripe dry Apricots	about 93 per cent.
,, Plums	,, 92 ,,
,, Peaches	,, 86 ,,
,, Cherries	,, 85 ,,
,, Pears	,, 84 ,,
,, Figs	,, 79 ,,
,, Gooseberries	,, 37 ,,
Dry Rice	,, 90 ,,
,, Maize	,, 88 ,,
,, Arrowroot	,, 77 ,,
,, Potatoes	,, 76 ,,
,, Oatmeal	,, 70 ,,
,, Peas	,, 67 ,,
,, Beans	,, 67 ,,
,, Bread	,, 61 ,,
,, Milk	,, 21 ,,

If dry rice contains 90 per cent. of starch, dextrin, and sugar, and potatoes contain 76 per cent. of starch and dextrin, and if all the starch and dextrin pass off in the urine as sugar, it is evident that to forbid potatoes and to allow instead an equal quantity of rice is simply ordering the quantity of sugar from this source in the urine to be increased 14 per cent., thus adding to the thirst and waste. Or if half-a-pint of port wine is forbidden, containing from 128 to 272 grs. of sugar, and if a pint of porter or stout is ordered, which contains from 368 to 960 grs. of sugar, it is clear that the quantity of sugar in the urine will thus be increased from half-an-ounce to an ounce and a-half daily.

Before passing to the best diabetic diet, there are two substances—bread and milk—which require to be further mentioned here.

Ordinary bread contains water, salts, starch, dextrin, sugar, and gluten.

If the salts, starch, dextrin, and sugar are washed away, the gluten remains, which, in a chemical point of view, is as unobjectionable as meat.

In making the different kinds of gluten bread this washing is more or less perfectly performed.

In the following analysis the water, starch, dextrin, and

sugar were determined, the residue or difference was taken as gluten:—

	Water.	Starch and Dextrin.	Sugar.	Gluten.	
Ordinary bread	36	40	1	23	per cent.
Aerated bread	37	42	2	19	„
Gluten bread from Toulouse .	2	16 to 44	0	82 to 54	„
Dried bread	2	60	1	37	„

The best washed gluten bread contains less starch than bran cakes or any brown bread; Dr. Pavey's almond bread is free from all starch, but the almond flour must be well washed to remove the sugar and dextrin, of which ten per cent. are present.

Badly-washed gluten may be made into dry bread containing bulk for bulk more starch than ordinary undried bread; thus an excess of gluten bread may keep up the amount of sugar in the urine, and prevent an improvement in the symptoms.

With regard to milk, one hundred parts may be taken to contain three parts of lactine, or about half-an-ounce of lactine exists in a pint of milk. If all of this animal sugar was incapable of being consumed in the system, milk would be nearly as injurious as an equal quantity of many wines, and the best sweet ale; but experiment shows that this sugar is often partly or entirely consumed.

A diabetic patient lived upon butchers' meat alone for two days. The quantity of urine passed was forty ounces the first, and forty-two ounces the second day; specific gravity, 1029·0. No trace of sugar could be found. He then took milk for two days; the first day eighty-eight ounces, the second day ninety-nine ounces. The urine was forty-five and a-half ounces the first day; specific gravity, 1024·1: and the second day sixty-nine ounces; specific gravity, 1011·9. Sixty-seven grains only of sugar were passed the first day, and twenty-three the second day.

At a more advanced period of the disease, when strictly animal diet did not cause the sugar to disappear from the urine, milk alone was again taken.

The first day 138 ounces of milk were drank; the urine

was 61 ounces; specific gravity, 1030·5. The second day 88 ounces of milk were taken; the urine was 34½ ounces; specific gravity, 1027·8. The quantity of sugar in the urine was 854 grains the first day, and 414 grains the second day. At this time, on animal diet alone, one day 280 grains of sugar were passed, and the next day 600 grains.

Thus milk is more or less injurious according to the stage of the complaint. When animal sugar can be consumed milk is comparatively harmless.

In the advanced stages of the complaint curds or sour milk, with the acid nearly neutralized by potass, soda, or ammonia, would be as unobjectionable as gluten bread.

The following *carté* of the dishes suitable for diabetic patients is given by Professor Bouchardat to those who consult him; and with a few alterations I consider it as much superior to any table I could draw up as French is to English cookery.

ENUMERATION OF THE DISHES SUITABLE FOR DIABETICS, ACCORDING TO THE OPINIONS PUBLISHED BY M. LE PROFESSOR BOUCHARDAT IN HIS 'MEMOIR ON DIABETES.' Paris, 1859.

Important Remarks.

The farina of wheat and every kind of flour made from cereals or leguminous vegetables—in short, all farina must form no part of any sauce; also raspings of bread. The farina of Martin, or the powder of gluten bread of Durand, or more simply the yolks of eggs, butter, or cream, must be used instead.

Sugar, caramel, carrots, onions, turnips, are also forbidden.

All leguminous vegetables must be washed repeatedly, and, if possible, they should first be well dried and chopped up small.

Rochelle salt may be substituted with advantage for common salt in the seasoning of food.

The dishes marked with a query are only fit for some patients. The urine should be analyzed after their use. (They should not be taken without express permission.)

Bread.

Slices of gluten bread of Durand of Toulouse.

The same heated in an oven.

The same made of bran.

Various kinds of bread prepared with Martin's gluten farina when gluten bread is not to be had.

Soups.

Consomme without bread.
Broth without bread.
Cabbage soup.
Leek soup.
Poached egg soup.
Bisque soup without bread or flour.
Game soup.
Broth with cheese and olive oil.
Semolina soup. The semolina made from the gluten of Durand.
Vermicelli soup. The vermicelli made from the gluten of Martin.
New paste soup from the gluten of Durand.
Soup made from granulated gluten of Martin.
Soup with butter and semolina of the gluten of Durand.
Soup with butter and the pure gluten of Martin.
Soup with olive oil, garlic, sage, with semolina of gluten, or with pure granulated gluten.
Yolks of eggs and cream may be added to these four last soups.

Hors d'Œuvre, Warm.

Fresh eggs, sausages, cabbage sausages, sour kraut sausages, truffled sausages.

Pickled pork with cabbage, also with sour kraut. These should be washed in much water and well dried.

Pigs' feet à la Sainte Menehould (?), or stuffed with truffles (?).

Black pudding. Ham. Ham and spinach.

Roast pork. Pork cutlets, fresh, simply dressed, or with mustard sauce, or with sauce piquante.

Forced meat balls of Troyes (?).

Fresh herrings with butter, or with sauce piquante. Dried herrings.

Fresh sardines. Fried oysters. Oysters dressed in the shell.

Hors d'Œuvre, Cold.

Oysters, white, English, Ostend, Marennes, and pickled.

Butter.

Pickled mackerel. Anchovy salad. Sardines pickled in oil. Salt herring with olive oil.

Olives. Stuffed olives. Artichokes with pepper.

Half slice of melon (???).

Ham salted or dried. Bayonne ham with jelly.

Lyons or Arles sausages. Bologna sausages. Troyes sausages.

Tongue. Wild boar's head. Prawns. Caviar. Lobster. Craw fish. Crabs.

All butchers' meat or pork smoked or salted with nitre and salt agree very well. They should have the salt removed by water, and be served in dry slices with olive oil or fines herbes.

Beef.

Boiled beef; with marrow; with cabbages; with well-washed sour kraut; with sauce piquante; with vinegar.

Beef-steak; with water-cresses; with beans; with anchovy butter; with Parmesan cheese; with cauliflower; with spinach; with chicory.

Roast beef; with the same things.

Fillet saute dans sa glace; with olives; with anchovy butter; with dry Madeira; with truffles; with pickle sauce, à la Bearnaise.

Minced beef with piquante sauce, or ribs of beef with the same.

Slices of palates of beef. Tongue with sauce piquante. Strasburg beef.

Lambs.

Larded lamb. Lamb sweetbread with truffles. Lamb chops.

Lamb with asparagus points; with spinach; with chicory.

Fricasee of lamb with mushrooms, without flour. The same with truffles.

Leg of lamb. Breast of lamb with aromatic herbs.

Mutton.

Leg of mutton. Mutton chops. Cutlets with mushrooms or truffles; with crumbs of semolina of Durand; with chicory; with spinach; with beans; with asparagus tops, à la Provençale.

Fillet of mutton pickled like a kid.

Small fillets grilled.

Kidneys on the skewer, or dressed with Malaga.

Breast of mutton with chicory.

Lambs' feet "à la poulette," without common flour (?).

Veal.

Sweetbread larded with gravy; with chicory; à la financiere with truffles; à la poulette (butter, yolks of eggs without farina).

Mesentery of the calf in oil (very good).

Frieandeau in gravy, or with chicory, or spinach, or lettuce, or French beans, or asparagus tops.

Calves' ears, plain.

Calves' head, plain or as mock-turtle (?).

Calves' brains, with butter, or à la poulette, or fried with gluten flour.

Tongue in paper.

Cutlets in paper or grilled plainly; with truffles or mushrooms; with ham; with asparagus tops, chicory, or lettuce.

Veal kidneys. Omelette of veal kidneys.

Cold veal with jelly.

Entrées of Poultry.

Fowl or capon with coarse salt; with jelly; with oysters; with Tarragon; with broth or fricaseed with gluten flour; "à la tartare;" with truffles or mushrooms; with lettuce.

Chicken salad (?). Mayonaise of chieken (?).

Capon or duck with olives. Slices of goose with olives.

Pigeon à la crepaudine, with Durand's semola.

Gelantine of poultry.

Entrées of Pastry.

All these dishes should be prepared with gluten flour instead of ordinary flour, the best butter, and very fresh eggs.

Vol au vent of poultry; of sweetbread with truffles or mushrooms (?); of salmon, turbot, or codfish.

Petit pâtes with gravy; with ham, lobster, prawns, and oysters.

Entrées of Game.

Partridges in cabbage, or en salmis.

Fillet of partridges with truffles.

Woodcocks en salmis, or with truffles.

Snipes en salmis. Wild ducks and larks en salmis. Larks with bread crumbs.

Larks "en caisse," also quails. Quails with lettuce. Teal en salmis.

Fillet of venison with peppered sauce, or with mushrooms.

Venison cutlet with truffles. Haunch of venison with sauce piquante.

Partridge salad. Purée of game with poached eggs.

Hashed hare.

Eggs.

Eggs beaten up. Eggs with Parmesan cheese, broiled with asparagus tips, or with truffles.

Poached eggs, with butter, with gravy or chicory, with spinach.

Omelette aux fines herbes, with truffles, with ham or sausage, with kidneys, with different kinds of cheese.

Omelette with hashed game.

Fried Fish.

In frying, ordinary flour should be replaced by gluten flour.

Fillets of sole. Plain sole. Whiting. Gudgeon. Smelts. Carp.

Fried oysters. Carp's roe. All fried fish. Fried legs of frogs. Fried crabs' tails.

Entrées of Fish.

Pike with caper sauce or oil.

Barbel "au bleu" with caper sauce or oil.

Trout. Barbel. Chub. Perch. Tench. Chub roasted with butter and herbs.

Dabs with caper sauce or oil. Turbot with capers or oil, with crumbs of semolina of Durand.

Turbot with lobster or oyster sauce. Salmon with capers or oil, with lobster or oyster sauce.

Salmon trout with capers or oil. Mayonnaise of salmon.

Sole aux fines herbes and au gratin with Durand's semolina. Sole matelotte Normande (?).

Fillets of sole en mayonnaise. Whiting with white wine and fines herbes. Fillets of whiting au gratin.

Mackerel à la maître d'hotel. Smelts au gratin with Durand's semolina, and aux fines herbes.

Matelotte of carps or eel. Carp "au bleu," or with oil.

Eel à la tartare, or à la poulette. Mackerel roe en matelottes.

Herring, with butter, or oil, or mustard sauce.

Cod fish à la maître d'hotel, or à la Provençale, or with oil.

Ray with butter or caper sauce. Sea eel with oil or butter. Brill. Cod with oil or butter.

Mussels à la poulette or pickled. Frogs. Lobster salad. Crabs. Prawns; or crab sausages.

All the sauces should be prepared with butter and the yolks of eggs, without flour or with gluten flour.

Salads.

Plenty of oil should be used and little vinegar, or it may be replaced by wine.

Lettuce with or without eggs. Romaine. Escarole. Chicory. Monks' beard.

Corn salad. "Scorsonere."

Watercresses. Celery (?). Green haricots. Cauliflower alone or with eggs.

Roasts.

Fillet of beef larded or roasted. Fillet of horse. Loin of pork.

Leg of mutton or lamb. Roast veal. Venison. Fowl or capon roasted.

Roast pigeon, duck, goose, turkey. Truffled turkey or capon.

Pheasant. Red or grey partridge truffled. Ortolan. Quail. Ruddock.

Snipe. Woodcocks. Thrush. Quails. Golden plover. Teal. Becfigues.

Several of these dishes may be garnished with watercresses, or chicory, or lettuce, or mushrooms, or bread of Durand's gluten in place of bread crumbs. Slices of gluten bread may be soaked in olive oil.

Entrémets of Pastry and other things to take the place of Confectionery.

Gluten cake made as follows:—Something more than three-quarters of a pint of water; three and a quarter ounces of very fresh butter; a sufficient quantity of salt or bicarbonate of soda are mixed and made to boil; remove them from the fire, and add rather more than eight ounces of flour of gluten; mix them well; beat them well on the fire to obtain a stiff paste; withdraw them from the fire, and let them cool for five minutes; then add, stirring violently, three very fresh eggs; divide into little cakes the thickness of the finger and the size of a plate; bake them in a slow oven for about half-an-hour.

Pancakes au gluten with Martin's flour and goose grease, or with semolina of Durand.

Wafers with flour of gluten or semolina.

Rum or Kerch jelly, or coffee jelly without sugar. Rum omelette without sugar with a little gluten flour.

Vanille omelette without sugar.

Light pastry answers very well with gluten flour, but sugar must be replaced by salt. In some cases the liquid part of the best honey, from which the solid injurious part has been removed, may be taken (?).

Gluten bread made with gluten flour. Take two pounds and a quarter of

gluten flour; fresh yeast the size of a filbert, mixed with a little cold water; two pinches of kitchen salt; hot water at 96° F. (35° C.) to 104° F. (40° C.), in quantity sufficient to make a thin paste, which is to be put in a pan powdered with gluten flour or bran, and then kept in a warm place until it has raised. This may take from an hour to two hours, according to the heat. Then divide this paste, using gluten flour, into little rolls, which are to be baked like ordinary bread. When there is constipation, one-quarter the amount of bran may be added to the gluten flour.

Entrémets of Vegetables.

Artichokes with butter; same without flour, or with oil; or à la Barigoule; or fried, or à l'Italienne; or à la Lyonnaise, without flour.

Cauliflower with sauce, either oil or gravy; au gratin, with Durand's semolina; with Parmesan.

Cabbages with butter or oil. Brussels sprouts with butter and oil. Lettuce with gravy or cream.

Asparagus with same or oil. Mushrooms with gluten semolina. "Salsifis" with sauce or gravy.

"Cardons" with gravy or marrow. "Morilles à la poulette." Truffles with Madeira or à l'Italienne.

Cucumbers well washed, or à la Béchamel with gravy or marrow. Celery with gravy, well washed.

Carrots cut very small, washed with much water, with gravy of meat.

All these vegetables should be washed by making them boil with the greatest possible quantity of salt water and drying them well.

Sweet vegetables, such as radishes, onions, turnips, may be used if they are cut very small and boiled with much water, and then well dried.

Coffee—Tea.

Mocha, slightly roasted, made with cold water without sugar. The same with cream, rum, brandy, and Kirsch.

Bourbon and Martinique coffee without sugar.

Pekoe tea à pointes blanches without sugar. Souchong.

Cream, rum, brandy, Kirsch may be added to the tea instead of sugar.

Petals of orange flowers, make like tea, without sugar.

Dessert.

Cream cheese without sugar. Neufchatel cheese, "bondon raffiné."

Cheese de Brie, d'Epounessés, or Auvergne, or Mont d'Or, or Gruyere, or Dutch, or Rochfort, or Pont Lévêque, or Chester, or Parmesan, or Stilton, or Silton, or Strakeno.

All should be dried, and without sugar.

In very rare cases, strawberries (?), peaches (?), raspberries (??), gooseberries (??), cherries (??), may be taken without sugar, either preserved by Appert's process or in brandy.

Fresh almonds, nuts, walnuts, young green walnuts in salt water without vinegar; the same dried.

Raw apples (??) and pears (??) may rarely, if ever, be taken.

Liqueurs.

Eau de vie de Cognac, de Mare. Kirschwasser. Jamaica rum.

Alcohol of Garus, diluted with orange-flower water, without sugar. Gin without sugar. Absinthe without sugar.

Wines.

Red.	*White.*
Avallon-Tonnerre.	Madeira.
Mâcon.	Marsala.
Beaune.	Chablis.
Côte Saint Jacques.	Pouilli.
Pomard—Nuit, old.	Girolles.
Chambertin—Clos Vougeot.	Nauchévre.
Châinette.	Mont Rachet.
Romanée.	Grave.
Hermitage.	Sauterne.
Bordeaux.	Côte Rôtie.
Médoc.	Hermitage.
Château Larose.	Sherry.
Saint Julien.	Rhine (?).
Château Lafitte.	
Cahors—old.	

The following general statement regarding the amount of sugar in wine and beer may be useful :—

			Amount of Sugar in an ounce of fluid. Grains.		Grains.
In Sherry I found the	sugar	varied from	4	to	18
Port	,,	,,	16	,,	34
Madeira	,,	,,	6	,,	20
Malmsey Madeira	,,	,,	56	,,	66
Tokay	,,	,,	74		
Samos	,,	,,	88		
Paxarette	,,	,,	94		
Cyprus	,,	,,	102		
Champagne	,,	,,	6	to	28
Sweet cider	,,	,,	18	,,	44
Bitter ale	,,	,,	12	,,	130
Porter	,,	,,	23	,,	40
Stout	,,	,,	45	,,	64

The fluids examined may be arranged in the following order, commencing with those which contain no sugar, and ending with the most saccharine :—

Geneva, Rum, Whiskey, Brandy, Claret, Burgundy, Rhine, Moselle ; these have rarely any sugar. Sherry, Madeira, Champagne, Port, Cider, Porter, Stout, Malmsey, Ale, Tokay, Samos, Paxarete, Cyprus have little or much sugar.

There are two great ends to be gained by the use of medicines in diabetes.

Of these the first and most important is to promote the oxidation of the sugar; or, failing this, to compensate the system for the loss of saccharine fuel and the consequent loss of power and nutrition by promoting the supply and oxidation of the oleaginous fuel.

Of all the medicines that can be given for the promotion of the oxidation, whether of sugar or fat, in the body, iron and alkalies are the most energetic; and hence, beyond all other remedies, iron or the ammonio-citrate of iron with excess of ammonia, or with other alkalies, are usually the best medicines for diabetes. The iron may be given in potass or Vichy, or in Fachingen water, and that preparation which confines the bowels least is most to be preferred. Hence the potassio-tartrate and Griffiths' mixture are often useful.

Alkalies without iron promote oxidation. This is very evident in the copper test for sugar. M. Miahle even has stated that alkalies are the specific for diabetes; without doubt they are of importance in promoting oxidation. Soda or potass may be given in the caustic state or as carbonates. Even carbonate of ammonia in ten, fifteen, or twenty-grain doses thrice daily in any gaseous mineral water lessens the thirst.

Long since Professor Graham tried the phosphate of soda, with three equivalents of soda, on the ground that the blood required this substance and could not get it in the animal food. I have not found any great advantage from its use.

Vichy water, more particularly the Celestin, is recommended by M. Bouchardat. It contains between eighty and ninety grains of carbonated alkali and alkaline earths in a quart of water. The Hospital spring contains about ninety-six grains, the Grand Grille ninety-two, the Hautrive eighty-nine, and the Celestin eighty-five grains to a quart of water.

Carlsbad Sprudel water and the more aperient Muhl spring is highly praised by Dr. J. Seegen. It contains about one-fourth or less of the alkali of Vichy water; but half a drachm or more of sulphate of soda in each quart gives an aperient action which the common salt of Vichy water rarely possesses. Marienbad Kreutzbrun water is twice as aperient, but rather less alkaline than Carlsbad Sprudel. Fachingen water has

one-third or more of the alkaline power of Vichy. Seltzer water one-sixth.

Besides alkalies some animal substances are thought to promote change in the sugar in diabetes. Of these, rennet and pepsine may be mentioned. In 1852 Dr. James Gray published some remarkable results in the 'Edinburgh Monthly Medical Journal,' p. 396, but I am not satisfied that rennet is very useful in diabetes. It is an albuminous substance in a state of change, and, therefore, it exactly fulfils the conditions required in the undiscovered specific for diabetes. It should be well washed with water to remove the adhering sugar and dextrin, and it should be given on an empty stomach, so as to enable it if possible to act on the sugar in the blood rather than on the sugar in the food.

Pepsine is another albuminous substance in a state of change. Its action in the stomach is to help the solution of the albuminous food, but when it passes into the blood it might be the animal diastase that carries on the change in the sugar. With this idea it has been given in diabetes, but with no satisfactory result; although many patients have said they were better whilst taking this remedy, yet I have never found the sugar diminish under its use. It sometimes helps the action of the bowels.

Lately oxygen gas has been tried by Dr. Richardson in diabetes. It would be splendidly simple if this were the specific for diabetes. This view implies that a deficiency of oxygen is the cause of diabetes, but the chemistry of the disease has not yet reached to this explanation.*

Vegetable and animal oils and fats constitute important remedies in diabetes. Of all these, cod-liver oil and cream are most frequently used. The following case may be taken as an instance of the amount of cod-liver oil that can be given:—

A man, aged 24 years, was admitted into St. George's Hospital, having lost two stone in weight during eight months. He passed seven quarts of urine daily. He remained under

* The latest experiments of Petterkoffer and Voit on the respiration in diabetes show that far less oxygen is taken in than in health.

treatment for a month, during which time he was on animal diet and cod-liver oil. He began with half an ounce daily, and this was gradually increased up to eight ounces. The quantity of urine fell to two pints and a-half, specific gravity 1030, and he increased in weight from 8 st. 8 lb. to 9 st. 1 lb.

Cream may be given in any quantity until the tongue begins to be coated, then it soon disagrees, and the stomach refuses to take it, or rejects it when taken.

Fats combined with alkalies, as soaps, are more ready to undergo oxidation than when the glycerine is unseparated. Pure glycerine is, however, often employed as a substitute for sugar in tea and in other liquids.

To lessen the thirst and the craving for food opium is very useful. The alkaloids of opium diffusing out of the blood and coming in contact with the nerves of the blood-vessels cause contraction of the capillaries; this affects secretion, so that the quantity of urine, saliva, bile, and intestinal secretion is greatly diminished. The drain of urine and the desire for food are thus checked, but the increased constipation and dryness of the mouth almost, and in some instances quite, counterbalance the gain obtained by checking the flow of water. By the use of very small quantities of opium, as five or ten grains of Dover's powder, or five or ten drops of laudanum once or twice daily, the thirst and excessive flow of urine may be stopped, and the constipation may not be excessively increased.

The second great object in the treatment of diabetes is to remove the constipation.

The excessive determination of water to the kidneys causes increased dryness elsewhere, hence the mucous membrane and the skin are harsh and dry; probably also the production of acid being greatly diminished by arrest of change in the sugar, the healthy secretion by the intestines and skin cannot take place.

Notwithstanding the amount of food eaten, the action of the bowels usually is very difficult. All saline aperients increase the thirst and pass off by the urine. Magnesia, from the absence of acidity, is usually inactive. Castor oil is by far the best aperient, when it does not nauseate, then

capsules containing castor oil with minute quantities of croton oil are most efficacious. Compound extract of colocynth with jalapine, scammony, or gamboge, or podophylline will act when oil cannot be taken. With regard to the action of mercury; when soluble it combines with the albuminous matters with which it comes in contact, and probably sets up increased chemical action. We see the nutrition of the parts to which it is directly applied, or carried by absorption and diffusion, is so altered that increased action, inflammation, and ulceration are produced. This altered nutrition has little influence on the oxidation of the sugar or fat, and hence diabetes is not benefited by mercury. Calomel may be used as an aperient, but it has not any advantage over other chemical or mechanical irritants to the mucous membrane of the bowels.

In extreme cases, the constipation of the bowels becomes the most serious symptom. The chemical disease leads to a mechanical difficulty amounting almost to an obstruction of the bowels. Strong chemical irritants are required to excite the muscular action, sometimes even "croton oil" is necessary. When the bowels do act the prostration of the strength is sometimes alarming; so little power seems to be set free in the body that any extra expenditure seems to deprive the heart of the force necessary to carry on the circulation, in the same way as a fatiguing journey or extreme mental anxiety will bring a prostration of strength from which with difficulty recovery will take place.

On the Loss of Mechanical Power Caused by Diabetes.

Loss of chemical action necessitates loss of heat, mechanical power, and healthy nutrition; neglecting the loss of power consequent on deteriorated structures, some estimate of the loss of power in those who suffer from diabetes may be obtained by calculating the amount of carbon which escapes in twenty-four hours in the sugar unoxidized.

In extreme cases from twenty to forty ounces of sugar may be lost in twenty-four hours. This is equal to 8·4 to 16·8 ounces of carbon, and this if fully oxidized would generate a

force capable of raising from ten to twenty millions of pounds one foot high.

In diabetes if no other fuel but sugar was supplied to the human machine, it would rapidly cool and come to rest; the motion of the heart and lungs would stop; but fatty, and even albuminous food may partially or wholly supply the force which ought to be got out of the sugar. When the coals fail in the steamer, the wood of the ship itself may furnish the fuel necessary to keep up the motion. The body may waste to move the heart and the lungs, until the supply of power failing, or the use of it being too great, feebleness and exhaustion constitute a general mechanical wrong which terminates in the stoppage of all muscular motion.

In addition to this general mechanical disease, the feebleness of the chemical action in and around the capillaries tends to produce local congestions and imperfect nutritions; hence mortifications, low inflammations, effusions, tubercles, and wasted muscles may arise from the deficient chemical action in the body, consequent upon the want of oxidation of the sugar.

LECTURE IV.

DISEASES OF SUBOXIDATION.—ON ACIDITY, OR THE ACID DIATHESIS.

Acid and sugar, chemically, are as closely related as parent and child; and hence a great similarity exists between the symptoms that arise from an excess of sugar and an excess of acid. The nature of the acid disease, the symptoms it produces, the means of detecting it, the consequences it occasions, and the treatment requisite to cure it, are all essentially chemical questions. A most important difference, however, exists between the sweet and sour disease, namely, this: the sweet disease is mostly free from secondary mechanical diseases; whilst acidity continually gives rise to mechanical complaints. Two of these secondary mechanical, or mechanico-chemical, complaints — gravel and gout — are the frequent lot of those who, living more by nerve than by muscle work, disarrange the healthy balance between the carbon and oxygen which go in and come out of the body.

Acid is essential for the performance of the functions of the body. Without acid the albuminous food could not be dissolved; the excretions from the blood could not be safely removed. If no acid was produced in the body, there would be no digestion and no depuration of the blood, and probably bony matter would accumulate everywhere. The vinegar cruet is only less essential to man than the salt-cellar, because the animal machine is itself an acid factory. Very often more acid is made than is useful or beneficial; then chemical errors occur, and these set up mechanical diseases as surely as the effect of the cannon-ball depends on the combustion of the gunpowder. The mechanical results are vastly more serious than the original chemical action; but they are

directly proportioned the one to the other. As the motion of the mass depends entirely on the motion of the molecules, so the mechanical disease arises solely from the chemical disorder.

It would be useless, even if it were possible, to give a list of the mineral, vegetable, and animal acids, between carbonic acid ($\text{C}\Theta_2$) and uric acid ($\text{C}_5\text{H}_4\text{N}_4\Theta_3$), which may be formed from changes in the textures of the body, or from the food. It is far more important to consider how an excess of acid may arise or accumulate in the system. This may occur in two ways—1st, by over-production; and, 2nd, by insufficient evacuation. When these causes co-operate the excess of acidity reaches its maximum.

First, on the production of acid in the body from the textures and food.

The living human body is, chemically, a varying mass of more or less complex carbonaceous matter, each portion being exposed to the action of oxygen. The chemical products everywhere vary according to the substances acted upon, and according to the time during which the oxidation is continued.

Outside and inside the capillaries, in every part of the body, in cells and out of cells, chemical changes are taking place. The oxygen of the air, the organic fluid, the catalytic membrane, act and react each on the other; and the products of the chemical action are reabsorbed into the blood, or are thrown upon the inner or outer surface, to be taken up by the alimentary mucous membrane, or to be removed by the lungs, the skin, or the kidneys.

At present, the chemical changes which take place in the textures are very imperfectly known, and the variations of action which occur in health and disease are only beginning to be observed. The healthy muscle, during the circulation of the blood through it, has no acid reaction; but for a time after death chemical actions continue, and sufficient acid is produced, and remains unneutralized by fresh alkaline liquor sanguinis, so that markedly acid reaction can after a time be obtained. Even during life, in tetanus, sufficient acid may be

formed to give an acid reaction, and after violent epileptic convulsions excess of acidity may be found in the urine. Even the nerves and the electric organs of fishes show signs of acidity when the alkaline blood ceases to flow.

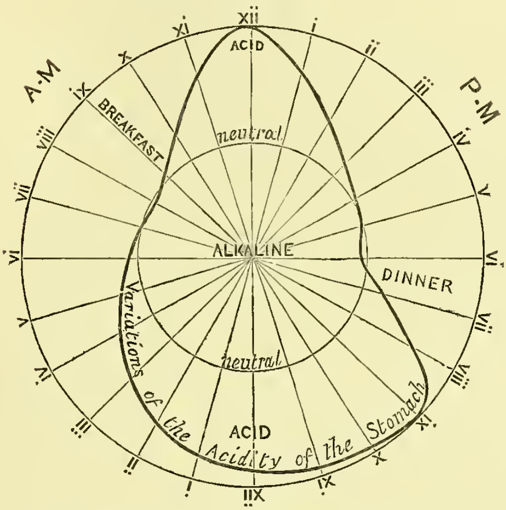
The production of some healthy though complex secretion may enable us, from its chemistry, to obtain increased clearness regarding the production of acid in the body. The gastric juice furnishes by far the most striking example of the formation of acid in the body. Until the chemical acid factory in the stomach is fully understood, the chemical changes which are going on outside the capillary vessels, as in the muscles, throughout the body cannot be realised.

There can be no doubt that the formation of gastric juice occurs outside the capillaries of the stomach. Its rate of secretion depends on the rate of passage of the blood through the capillaries; and this is directly under the control of nerves that open or shut the blood-vessels. In the fluid poured out of the capillaries chemical changes occur, acids are formed—perhaps Dr. Marcet's colloid acid; or by the oxidation of sugar, among lactic and other acids, oxalic acid may be produced, and this may decompose the chloride of sodium, and the most diffusible hydrochloric acid may be poured out on the free surface of the tubes; whilst the alkali passes with the organic acid, or its products of combustion, back into the blood.

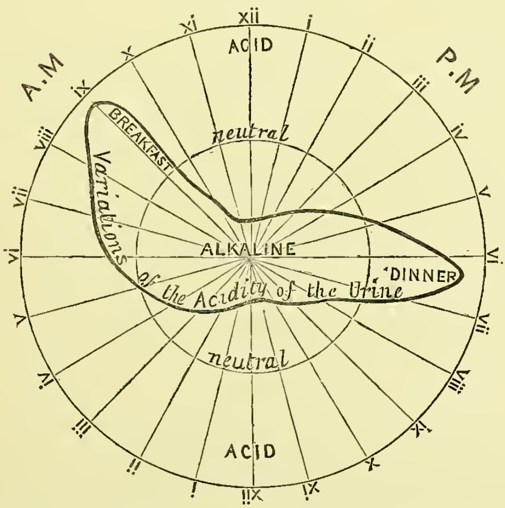
That the blood increases in alkalescence during digestion can easily be proved by careful observation of the secretion of urine before and after food, or by the effects of severe or constant vomiting. The following diagram will best show you the contrast which can be traced between the acidity of the gastric juice and the acidity of the urine. You will perceive that when the gastric juice is most acid the urine at that time is least acid, or most alkaline; and when all the gastric juice is absorbed, then the acidity of the urine is at its highest point.

In the Medico-Chirurgical 'Transactions,' vol. xxxv., p. 41, you will find a paper "On the Alkalescence of the Urine from Fixed Alkali in Some Cases of Diseased Stomach." I shall

Curve of variation of the acidity of the stomach.



Curve of variation of the acidity of the urine.



here give you only one example, in order to fix this inverse relationship of the acidity of the stomach and urine firmly in your minds. A man, aged 46, was admitted into St. George's Hospital with sarcinæ ventriculi. The eruption from the

stomach occurred at irregular periods, once and sometimes twice daily; the quantity vomited each time was from one to four pints of intensely acid fluid. The urine was usually passed about six times in twenty-four hours, when the vomiting was most. The urine was acid twice, or at most thrice, daily before the sickness occurred; and for the rest of the day after the vomiting the urine was strongly alkaline from fixed alkali. The patient remained in the house for a month, and during the last week he had only one attack of sickness; then the urine became markedly acid each time it was passed, and remained so throughout all the day.

After digestion is finished, when the food is dissolved in the stomach, the intensely acid fluid is in part returned into the blood. The serum might almost cease to be alkaline but for the neutralizing action of the bile; thus the degree of alkalescence of the blood must be continually changing, and the fluid effused from the capillaries, and out of which the secretions are formed, must become less alkaline after the food is absorbed than it is whilst digestion is going on in the stomach.

An oxidation similar to that which occurs in and around the stomach cells must occur to a greater or less degree everywhere throughout the body; carbonic acid or other acids arising from a less perfect combustion, must be formed outside the capillaries of the body. In the muscles and nerves, and in every other texture, power must be set free by the mutual action of the carbon and the oxygen, and the acid products would quickly neutralize the alkalescence of the blood if the acids did not pass off by the lungs, the skin, and the kidneys.

On the Removal of Acid from the Body.

Without cessation night and day free acid continues to pass into the air-vesicles of the lungs from the blood, thus rendering it more alkaline than it would otherwise be, and counterbalancing not only the acid produced by oxidation in the different textures, but also the residue of the acid from the gastric juice and food which is not neutralized by the bile.

If the combustion in the body were complete, the whole of the products, except the ashes, might escape by the lungs; free respiration might carry off readily all the acid produced in the system; but imperfect oxidations do occur, and then other acids besides carbonic acid are formed and give rise to neutral or to acid salts which are not volatile, and these being unable to pass off by the lungs are thrown out by the skin and the kidneys.

There can be no doubt whatever that acid is produced outside the capillaries of the skin and kidneys in the same way, although to a much less degree than in the stomach cells. The chemical composition of the substances that pass into the urine and the sweat depends not only on the amount of action of the oxygen, but also on the chemical composition of the fluid poured out of the capillaries to form the secretion.

If the serum of the blood is at its highest point of alkalescence, the acids formed by oxidation during the secretion of urine may be too feeble to neutralise the alkali poured out, and alkalescent urine may result. If, on the contrary, feebly alkaline or acid salts are effused from the capillaries, a very small amount of additional acid produced by oxidation in the secreting structure of the kidneys will set free some of the acid from the acid salts, and thus free uric acid may appear in the urine.

The same formation of acid occurs in the secreting structure of the skin, and although it is not possible to demonstrate the daily variations of the acidity of the sweat, yet the extraordinary increase in its acidity with strong exercise, or in some diseases, as in rheumatic fever, shows that it is subject to great variations.

The variations in the alkalescence of the saliva were long since shown by Dr. Wright to be influenced by the digestion. —*Lancet,* 1841, p. 787.

The smallest amount of acid is thrown out of the system when the respiration is impeded, whether from insufficient exercise or from imperfect supply of air; then carbonic acid accumulates, and the less perfect products of combustion are increased in the serum. If these can escape by the kidneys

and skin the system is relieved, and no secondary symptoms are produced; but if these vents are closed, and if by acid diet and an irritable stomach an excess of acid is poured into the blood, then an outburst must take place, and chemical and mechanical diseases — that is, unusual molecular or massive motions—occur until the healthy condition of the blood is again reached.

Excess of acidity or the acid disease may shortly be defined to be a want of free oxidation and an insufficient escape of the products of imperfect combustion.

On the Means of Detecting Acidity.

It is not easy for the physician to determine accurately the escape of an excess of acid by the lungs, and still less so by the skin; but by both chemical and microscopical evidence he can follow the minutest changes which occur in the acidity of the urine, and thus he may know something not only of the state of the blood from which that urine is secreted, but he may obtain some information regarding the activity of the processes of oxidation and nutrition elsewhere outside the capillaries. Different litmus papers vary so much in composition and delicacy of reaction that no satisfactory conclusion can be reached by this test alone. A standard solution of soda furnishes the surest chemical proof of the amount of acid in a given quantity of urine, and thus variations may be proved and comparisons made with the utmost accuracy. But a readier method of coming to a practical conclusion exists in observing by the microscope the state in which the uric acid exists in the urine. The delicacy of this test for free acid far surpasses any other; indeed, litmus paper and a standard solution cannot enable you to distinguish between acid salt and free acid; but the microscope, by showing more or less free uric-acid crystals, tells at once the greater or smaller amount of free acid in the urine. As long as free uric-acid crystals do not exist in the urine, no very great amount of acidity is present. When acid urates alone are passed there may be very great effect on the litmus; but as long as the microscope

and chemistry show that free uric acid is absent, the chief secondary mechanical disease, uric-acid stone, is not likely to be set up.

Hence the determination of the presence or absence of free uric acid in the urine is a question of great importance.

A small bottle or test tube should be filled with fresh urine and examined by transmitted light. Uric-acid crystals can be easily seen. If no red sand is present, in twelve hours another examination should be made. Very frequently a deposit occurs as the urine cools, then the microscope must be used to see whether crystals of uric acid are mixed with the granular deposit. The amount of free acid may be known by the rapidity with which the uric-acid crystals appear, by the size of the crystals, and by the more or less perfect decomposition of the granular urates.

When the free acid is in very great excess, the uric acid may crystallize in the renal tubes or in the pelvis of the kidney or in the bladder. When very little free acid and very little uric acid has been present, I have seen the crystals of uric acid appear on the eleventh day after the water was passed.

Professor Scherer long since stated that an acid fermentation took place in the urine soon after it was passed; but I have been unable to satisfy myself that any increase of acidity occurs. His experiments were not made on healthy urine. When he made them, the state in which the uric acid existed in the urine was not known. The slow deposition of uric acid from a feebly acid solution of urates was not taken into account.

Very frequently, when examining the same specimen of urine day after day for uric-acid crystals, I found that no free acid was deposited; until at last I was led to make exacter experiments to determine whether the free acid in the urine was increased after the water was made. But first a series of twenty-seven experiments were made on healthy urine to determine how often, and how soon on standing, uric acid crystallized out. Four times only were these crystals found by the microscope twenty-four hours after the water was

made; and five times the acid crystallized out in two days. Eighteen times no uric acid was found free. In other words, eighteen times out of twenty-seven the urine under the microscope did not show this evidence of an increase of acidity. In the other nine times the uric acid might possibly have been set free by an acid fermentation, although another explanation was probable, namely, that the crystals only formed slowly because no great quantity of urates were present, and because the liberating acid was very weak. For determining between these views, a standard alkaline solution of caustic soda was prepared, and the acidity of the urine was measured as soon as possible after the urine was made, and then from time to time afterwards the acidity of the same urine was again noted. Thus the following experiments were made:—

June 7,	Fifty cubic centimetres of healthy urine just passed were neutralized by	1·8	c.c. of standard solution of soda.
„ 10,	„	1·8	„
„ 12,	„	1·8	„
„ 14,	„	1·8	„
„ 17,	„	1·2	„
„ 19,	„	0·8	„
„ 13,	Fifty cubic centimetres passed by another healthy man neutralized by	1·5	„
„ 15,	„	1·5	„
„ 15,	Fifty cubic centimetres passed at different times neutralized	1·6	„
„ 17,	„	1·6	„
„ 19,	„	1·6	„
„ 21,	„	1·6	„

The total quantity of urine made in twenty-four hours was collected, and the acidity determined.

June 17,	Fifty cubic centimetres	neutralized	3·8	c.c. of standard solution.
„ 19,	„	„	3·8	„
„ 21,	„	„	3·8	„
„ 22,	„	„	3·8	„
„ 27,	„	„	2·6	„

These are examples taken from many others, all showing that no change in the acidity occurs for some days after the urine is passed, and that then the acidity diminishes.

When it was proved that sugar existed in small quantities

in healthy urine, I thought that some evidence for or against an acid fermentation might be got by determining the amount of sugar in the urine, first when fresh, and afterwards when it had stood some days.

Three litres of healthy urine were divided into two equal parts. The one half was examined for sugar immediately; and the amount of sugar was 2·4 grains. The other half was left for twenty-five days, until it became feebly alkaline, and then the sugar was determined, and the amount was 1·9 grain. A loss within the limits of error in the method of analysis.

These and many similar experiments are opposed to any acid fermentation; and when the formation of uric-acid crystals in the urine occurs, it may be taken as a proof that some free acid is secreted by the kidneys, and that this, sooner or later, has set free more or less uric acid from the acid urates in the urine.

The longest time in which I have seen uric acid crystallize out has been eleven days, but usually the first, second, or third day after the water is made the crystals form, if they form at all; and the formation of these crystals is the only certain and delicate test of the presence of free acid in the urine. I had hoped that the form of the crystals, varying as it does so greatly, might enable me to determine the nature of the liberating acid; but after a long series of experiments I can as yet come to no satisfactory conclusion in this respect.

On the Symptoms of Excess of Acidity.

As in diabetes, so in acidity, there are no symptoms when the disease begins. The over-acidity or the excess of sugar may come and go away without being observed. A little heartburn or a little urgency in passing water may last only for a few minutes, and be cured by nature as quickly as it was caused. Only when the skin or mucous membrane have become irritable by the continued action of the acid, do symptoms of acidity force themselves on the notice and

require medical aid. The amount of uneasiness or pain will vary with the sensitiveness of the membrane and with the degree of acidity. Slight degrees of acidity hardly irritate the skin ; but itching, nettle-rash, eczema, and herpes are the outbursts of an over-acid state.

The mucous membrane of the stomach is less sensitive than that of the pharynx, œsophagus, and bowels. When 162 grs. or even 81 grs. of dry tartaric acid in four or six ounces of water are taken, the acid hurts the mouth and the upper part of the food-tube, and then ceases to be felt for three hours or more, when it causes violent griping pain for an hour or two. When the mucous membrane has become irritable the stomach becomes much more sensitive, and acidity causes pain, cramp of the muscular coat, and vomiting ; the bowels feel more and move more strongly, and violent pain, colic, tormina, and tenesmus come on.

If the sensitiveness of the mucous membrane of the urinary organs is increased, the nerves and muscles become irritable ; urgency and frequency of passing water gradually increase into constant pain and violent spasm of the bladder. In the urethra a scalding pain is felt, and constriction of the mucous membrane causes a complete stricture whilst the spasm lasts.

When the acidity is excessive, the skin, stomach, and urinary organs may all be simultaneously irritated. In other words, the amount of acid formed may be so great that it is thrown out everywhere. Most frequently the acidity only shows itself in the stomach and in the urine ; and the symptoms produced in the stomach and urinary organs are so closely dependent that the same treatment that does good to the one mucous membrane will be found to do good at the same time to the other.

I might here, if time permitted, give you innumerable cases of acidity illustrating the great persistence and intractability of the deposit of uric acid, and its great liability to return as soon as the alkalies are omitted, unless the strictest diet is observed. This resemblance of these cases to cases of diabetes is very striking ; and, moreover, in slight diabetes or inter-

mittent diabetes the production of excess of acid is very frequently to be met with.

I must, however, give you two cases illustrating the rarer consequences of this excess of acidity. A gentleman, aged 40, consulted me for constant deposit of urates and uric acid in the urine. He had been subject to these deposits for years; for the last few months occasionally, from one to five hours after a late dinner, he was attacked by pain in the stomach, which in a short time became intermittingly spasmodic. The intensest pain was reached in half a minute, it then relaxed, and returned as badly as before in two minutes. His suffering lasted about an hour, when the pain gradually abated, leaving a tenderness on pressure and an irritability after food for two or three days. The urine passed after the attack gave on standing uric-acid crystals. I advised him when another attack occurred to fill the stomach with hot water and then to reject it. This he did, and a considerable quantity of nearly clear acid fluid was thrown up ; on repeating the emetic later during the same attack, a much more intensely acid chymous fluid was obtained, showing that probably an hour-glass contraction of the stomach had existed. By careful diet and anti-acid medicines the attacks entirely ceased. In another patient, six or eight hours after food, attacks of violent cramp used to occur in the rectum, and last from half-an-hour to an hour. Relief at the time was obtained by pressure on a hard seat; and by careful diet and alkalies the attacks entirely ceased.

Before speaking of the treatment, a few words must be said

On the Consequences of Excessive Acidity.

In all I have hitherto said of diabetes and acidity a parallel might be drawn between the two diseases, with this difference—that the bland sugar acts as a diuretic, whilst the irritating acid affects the nerves and muscles, causing pain and spasm ; but in the consequences of the two diseases an entire divergence must be noted. Diabetes causes a painless weakness and atrophy. Acidity is the cause of from

50 to 60 per cent. of all the cases of stone that occur in England. Dr. Prout says—"If a uric-acid nucleus had not been formed and detained in the bladder, two persons, at least, out of three who suffer from calculus would never have been troubled with that affection."—P. 583, 'Stomach and Renal Disease.'

In the 26th vol. of the 'Medico-Chirurgical Transactions' for 1843, I have given the analysis of the calculi in St. George's Hospital. In 233 calculi, 89 consisted of uric acid alone; that is, 38 per cent. of these stones were caused *solely* by acidity. Whilst 135 consisted of uric acid, uric acid and oxalate of lime together, and of these substances mixed with urates, that is, 58 per cent. were wholly or *partially* caused by acidity.

Gravel is still more frequently caused by over-acidity. Seventy-five per cent of all renal calculi are uric acid, caused by acidity alone. Hence three out of four renal attacks, giving rise to almost as violent mechanical suffering as the human body can endure, are caused by a slight chemical disorder which often continues unobserved until the mechanical disease is set up.

On the Treatment of Acidity.

The relation that exists between diabetes and over-acidity is even more evident in the treatment than in the causes and symptoms of these diseases. The best diet for diabetes is the best diet for over-acidity. The same medicines are most useful in both complaints. The same immediate effect can be produced by treatment, and there is the same disposition to a relapse after the symptoms have entirely ceased when wrong food is taken.

The treatment of acidity must be considered under two heads: First, the diet; and secondly, the medicines.

With regard to the diet. All that has been said against saccharine and farinaceous diet in diabetes might be repeated here, inasmuch as these substances give rise in the system to various acids in their progress to carbonic acid and water.

Hence, as regards the action of sugar, dextrine, and starch, I may refer to the lecture on diabetes; but as the acid diathesis arises [from a slighter check to the oxidizing actions of the body than the saccharine diathesis, therefore a less strict diet will give a greater improvement in this disease than in diabetes. Moreover, medicines effect a more decided good in over-acidity than in the saccharine complaint, and on this account, also, greater liberty may be given in diet provided the acidity from the food is neutralized by alkaline medicine.

Another difference must be made in the diet of those who suffer from these two complaints. In diabetes, fatty substances, cream, butter, fat, and oil check the wasting of the body; but in excess of acidity these articles of food often give rise to great uneasiness in the stomach; they are very liable to cause a peculiar feeling of irritation, which is known as heartburn. Thus, over-acidity and heartburn often can be removed and kept away by leaving off sugar and butter. In severer cases, potatoes, rice, arrowroot, and a considerable portion of the daily bread must be given up. Fruits of all kinds are mostly highly flavoured ether mixtures of starch, sugar, and acid. Wines and beer chemically differ from fruit only by containing alcohol instead of some starch and sugar. Alcohol itself, very probably in the stomach as well as in the air, gives rise to acid, and the weak spirit and sugar of half-fermented beer and effervescing wine more easily undergoes this acid fermentation than fully fermented wine and pure spirit. Hence, in extreme cases of acidity small quantities of lean animal food, including fish, flesh, fowl, game, and eggs, and brandy-and-water, constitute the best anti-acid diet. All fluids containing sugar should be avoided; and alkaline gaseous mineral water, natural or artificial, will neutralize a portion of the acidity which the imperfect combustion continually produces.

Exactly the opposite diet was advised at the dawn of animal chemistry, on the ground that the ash of vegetables containing alkalies, these would neutralize all the acid that should arise from the starch and sugar. But take, for

example, potatoes: the amount of acid-producing substances in them is from 20 to 30 per cent.; the amount of alkali at most will not reach to 1 per cent. Or take bread: the ash of bread would neutralize at most 1 per cent. of acid. The amount of acid-producing substances in bread is 46 per cent. Any other fruit or vegetable would give equally good evidence against a vegetable diet in over-acidity.

The object of medicines in this complaint may be divided into—first, the removing, and secondly, the neutralizing of acid.

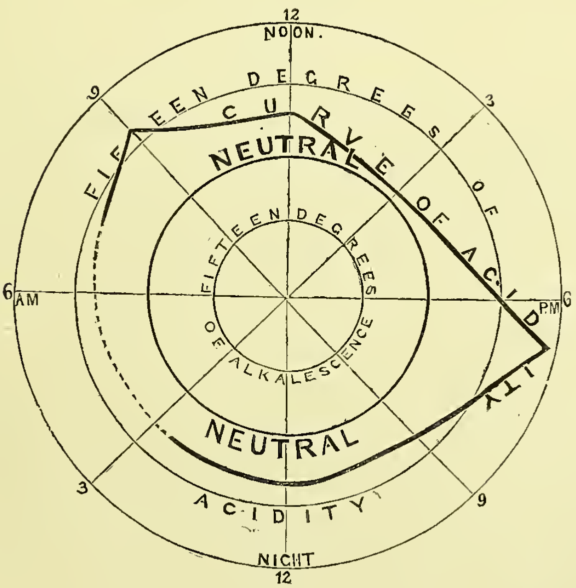
The removal of acid is effected most immediately and directly by emetics, emptying the stomach at the time when the greatest quantity of acid is present, that is, during the digestion of a full meal. In the treatment of the acidity of children, this is the shortest and readiest way. Hot water, mustard and water, ipecacuan will remove more acid than would be neutralized by the usual amount of alkali that would be taken daily. The repetition of the emetic should depend on the reappearance of uric.acid crystals in the urine.

The free action of the skin by baths, especially Turkish baths and vapour baths, removes acid quite as effectually, although more slowly, than by taking away the gastric juice. Moreover, an increased natural action disarranges the system less than a stomach catastrophe, which, though scarcely felt by the young, is a shock unfitted for advancing years. Among the different methods of exciting perspiration strong exercise must be mentioned, because this generally implies a freer respiration, and this means the greatest possible conversion of acids into carbonic acid and water. The more bracing the air is, and the more free from mechanical and chemical impurities in the form of dust, smoke of all kinds, fogs, and noxious gases, the more vivid is the combustion, and the greater is the amount of acid that is removed from the system through the lungs, but it must not be forgotten that every muscular contraction develops paralactic acid, so that the gain from increased exercise is diminished by the amount of acid thus produced.

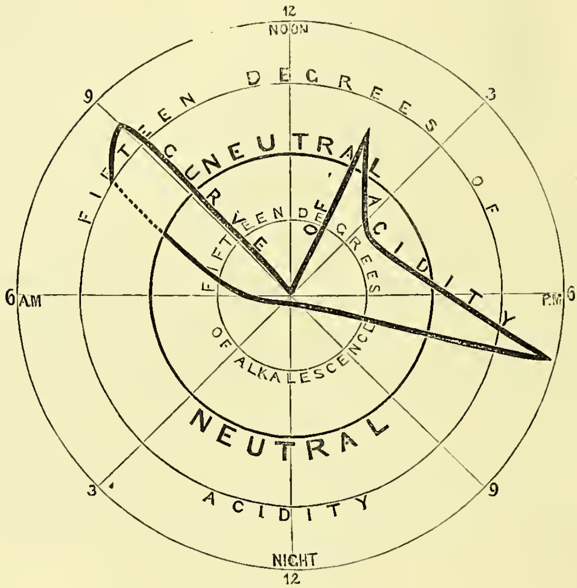
There remains to be considered the removal of acid by the kidneys. By increasing the action of the kidneys, an increased quantity of acids of many kinds, from carbonic acid to uric acid, is thrown out of the system. Diuretics thus become veritable anti-acids. Hence, pure water and nitre and mineral waters, by exciting diuresis, relieve the blood and textures of acid, but whilst promoting the action of the kidneys the acid may be neutralized; and this is the second object to be obtained by medicine.

In neutralizing the acidity of the urine, by far the most effectual medicines are vegetable salines, containing fixed alkalies or earths. The following diagrams of the acidity of the urine will show you better than any words of mine how differently salines containing volatile and fixed alkali act on the urine :—

Five drachms of tartrate of ammonia in the day.



Five drachms of tartrate of potash in the day.



Each degree of acidity or alkalescence was made equal to the twelfth of a grain of carbonate of soda. Although five drachms of tartrate of ammonia were taken in the day the urine was not made alkaline, not even neutral; whilst after the same quantity of tartrate of potass the urine was alkaline for the greater part of the day, and at one period reached as low as thirty-two degrees; in other words, a thousand grains of urine contained three grains of carbonate of soda. Moreover, eighty grains of carbonate of ammonia daily in three different experiments did not make the urine neutral, though it acts more strongly than most alkalies in neutralizing the acidity of the gastric juice in the stomach. Three drachms and a-half of liquor potassæ, containing 6¼ per cent. of potass, taken in one day, though it lessened the acidity, did not cause alkalescence; still, no doubt, the action of this and other alkaline remedies, when long continued, produces very decided effects in neutralizing acidity.

The comparative worth of equal quantities of different alkalies may be determined by their combining proportions.

Thus 10 parts lithia	= 12	parts	ammonia.
,, ,,	= 14	,,	magnesia.
,, ,,	= 19	,,	lime.
,, ,,	= 21	,,	soda.
,, ,,	= 33	,,	potass.
,, ,,	= 54	,,	bismuth.
,, ,,	= 25	,,	carb. of lithia.
,, ,,	= 27	,,	carb. of ammonia.
,, ,,	= 29	,,	carb. of magnesia.
,, ,,	= 35	,,	carb. of lime.
,, ,,	= 37	,,	carb. of soda.
,, ,,	= 48	,,	carb. of potass.
,, ,,	= 70	,,	carb. of bismuth.

In other words, fourteen grains of magnesia will neutralize as much acid as twenty-five grains of carbonate of lithia, or forty-eight grains of carbonate of potass, or seventy grains of carbonate of bismuth. One grain of carbonate of lithia is nearly equal to a grain and a half of carbonate of soda or two grains of carbonate of potass.

In ordering these different alkaline substances, their constipating or their aperient action must be considered; and beyond all this, the peculiarities of different individuals must be learnt by experience. That carbonate of soda to the amount of two ounces and a half daily may be taken for months with impunity may be seen in a case in 'Med.-Chir. Trans.,' vol. v., p. 80. The blood had a strong buffy coat. The urine was alkaline.

In speaking of the treatment of diabetes, I have dwelt on the alkaline action of different mineral waters; to this I must refer you for further information. But there is in the treatment of acidity an advantage in giving mineral waters which does not exist in the treatment of diabetes. In acidity pure water may be regarded as an anti-acid. It lessens the symptoms, and prevents the consequences of the acidity; where strong acid irritates, weak acid has no effect. Strong acid quickly sets free uric acid; whilst weak acid has to make up by time what it wants in force, so that

simple dilution, or the amount of water that exists in the mineral water, becomes an important means of relieving acidity.

When the acidity is excessive, all these different methods of lessening acidity must be used at the same time. To give acid in the food and to neutralize it by medicine is child's play, unless the amount of alkali taken exceeds the amount of acid eaten. The greatest possible effect can be obtained by stopping acid from going in, by removing acid by perspiration, and by the stomach, skin, and kidneys, and by neutralizing the acid by lithia, ammonia, magnesia, soda, or other alkalies.

LECTURE V.

DISEASES OF SUBOXIDATION.—ON THE OXALIC DIATHESIS.

On the Oxalic Diathesis.

Strictly speaking, the oxalic diathesis is included in the general expression acid diathesis, for the oxalic is only the last acid in the descending scale of ternary organic substances that is produced before perfect combustion sets free carbonic acid and water. Still I shall treat of oxalic acid separately, partly for the sake of clearness, and partly because, being a very strong acid, it will probably be found, in the progress of animal chemistry, to play an important part in the healthy chemical actions that take place in the body.

As oxalic acid is only a special instance of acidity, much that was said in the last lecture applies to the production of an excess of this acid also. To avoid useless repetition, I shall now confine myself to that which belongs specially to oxalic acid as distinguished from other acids.

The production of oxalic acid in the body is a purely chemical process. Certainly it would have escaped notice if the compound which it forms with lime had not been very insoluble in dilute acid. This chemical cause leads to the secondary mechanical disease, mulberry calculus, and this complaint is so frequent and so serious that the primary chemical disorder hence rises to an importance which it would not at all reach by itself.

To make the production of oxalate of lime depend on an oxalate of lime diathesis, so far, at least, as the lime is concerned, is only giving a hard word to the chemical affinity of oxalic acid for lime, which partly depends on the insolubility of the compound produced.

If perfectly healthy action is marked by the production of carbonic acid and water	CO_2H_2O
The first and slightest arrest of oxidation will be marked by the production of oxalic acid	$C_2O_3H_2O$
The higher degrees of arrest of oxidation of sugar and albumen will produce other acids, as acetic acid	C_2H_3OHO
Or hippuric	$C_9H_8NO_5HO$
Or uric	$C_5H_4N_4O_3$
The highest degree of arrest of sugar will give diabetes; grape sugar .	$O_6H_{12}O_6$

Hence, oxalic acid is related to over-acidity and to diabetes in that it is the lowest of a series of imperfect oxidations, whilst diabetes is the highest term of the same series. Moreover, it will be seen that between the oxalic and the saccharine diathesis there is a resemblance not only in the causes of these diseases, but also in the treatment.

Oxalic acid, like sugar, can arise from two sources—first, from the food; and secondly, from the textures.

Of all the acids that exist in the vegetable kingdom, the most widely present is oxalic acid. Schleiden even states that oxalate of lime, either in needles or octahedra, is present in every plant; in some, as in rhubarb or sorrel, oxalic acid is present in very large quantities. It is formed out of carbonic acid and water by part of the hydrogen of the water combining with the carbonic acid while the rest of the water and the oxygen are given off; thus, $C_2O_4H_4O_2 = C_2O_3H_2O + H_2O + O$. As this oxalic acid is mostly combined with potassa or lime, it is not likely to escape oxidation in the body before it passes out of the kidneys, and hence probably from this source oxalate of lime rarely occurs in the urine.

All the hydrocarbons, as starch and sugar, that exist in the food, and most of the vegetable acids, when oxidized out of the body by nitric acid or by fusion with hydrate of potassa, give oxalic acid; if fully oxidized, they would give carbonic acid and water.

In the oxidizing action which is going on in the body, the starch, sugar, and vegetable acids may all stop in their progress to carbonic acid and water before their final change takes place, and thus give rise to oxalic acid; and this will combine with any lime that happens to come within its reach, and will pass out as oxalate of lime in the urine. Moreover,

in addition to these vegetable sources of oxalic acid, there may be two sources from animal substances. The sugar that has its origin in the muscles and in the liver may, by arrest of oxidation, furnish oxalic acid.

Moreover, there can be no doubt that albuminous substances, whether of vegetable or of animal food, give rise to uric acid when an excess is eaten; and when uric acid is imperfectly oxidized, it divides into oxalic acid and urea; so that oxalic acid may be produced even from the albuminous constituents of the different organs and textures themselves. In the process of disintegration different portions of the albuminous matter may stop at different degrees of oxidation, when from any cause that action is incomplete. Hence uric acid, or urea and oxalic acid, instead of urea and carbonic acid, may be thrown out of the body. Thus, then, there may be not less than four sources of oxalic acid in the urine—two in the food and two in the textures.

That oxalic acid does come from the textures is rendered more likely by the fact that when the strictest possible diet is observed oxalate of lime may occasionally still be detected in the urine. In this respect, as in others, the parallel with diabetes is very close; the difference being that the sugar causes diuresis, and implies a greater loss of force, whilst the oxalic acid, in consequence of the insolubility in dilute acid of the oxalate of lime, may give rise to a serious mechanical disease, which requires severe mechanical treatment for its cure.

It is highly probable that oxalic acid, though not so widely diffused in animals as in vegetables, may be much more frequently present in different secretions and textures of the body than is yet proved to be the case. Already it has been found in the blood, in mucus, in saliva, and in perspiration. Its occurrence in the urine implies no disease, but only a slight error of deficiency in the oxidizing actions in the body.

It is twenty years since I was consulted by a medical gentleman, who said he had been greatly alarmed by being told that the oxalate of lime in his urine indicated serious

and, possibly, malignant disease. I advised him to examine the water passed by apparently healthy people. In a very short time he wrote to me that he found octahedral crystals in the urine of the most healthy of his friends.

On the Means of Detecting Oxalic Acid.

At present oxalic acid is most readily detected by means of the crystals it forms with lime. It requires no skill and no preparation of the urine to find the oxalate of lime. The urine should be left to stand for twenty-four hours in a bottle or tall glass; the upper part of the fluid should be poured off, and the last few drops remaining should be examined. A magnifying power of 320 times is generally sufficient, but the crystals are sometimes so small that more than this power is necessary to determine the form. Generally oxalate-of-lime octahedra are thus found without the least difficulty—sometimes in large single crystals, very frequently in aggregations of small octahedra forming microscopic calculi.

Dr. Golding Bird was the first who stated that these crystals, which had for some time previously been observed in urine, were oxalate of lime.

It is only in rare cases that so many crystals can be collected from the urine as will furnish the chemical proof that these octahedra are oxalate of lime; but this proof has been obtained. Moreover, artificially-formed oxalate of lime, which is generally an amorphous powder, can be made to crystallize in octahedra by dissolving it by the aid of heat in very dilute hydrochloric acid, and setting it aside for many days, when octahedral crystals will very frequently be formed. The less oxalate of lime present and the more acid the solution the slower the crystals form. In no experiment have I succeeded in forming the crystals which Dr. G. Bird has called dumb-bell crystals of oxalate of lime. They do not very frequently occur in the urine, and I cannot say that their appearance gives any important indication. Oxalate of lime occurs in the urine in a third form, which M. Donné has also observed; and as the microscopic appearance may lead you to a wrong diagnosis, it requires to be mentioned here.

I sometimes find, with or without octahedral crystals, little flattened discs, nearly the size of very small blood-globules. When rolling over, they may very easily be mistaken for blood-globules. They vary much in size, some being much smaller than any blood-globules. I have seen these discs mixed with octahedral and dumb-bell crystals—in fact, the smallest dumb-bell crystals form minute flattened discs. They are not soluble in water as blood-globules are ; they have a different appearance in the centre, and the eye, by practice, can learn to distinguish certainly between blood-globules and this form of oxalate of lime.

On the Symptoms of the Oxalic Diathesis.

The most common symptom of the oxalic acid diathesis is flatulent dyspepsia; frequently before food considerable uneasiness is felt, and eructation occurs. Eating for a time removes the symptoms, often only to return in an hour or two with increased intensity. The pain sometimes is so severe, persistent, or intermitting, that it can only be produced by actual cramp of the muscular coat of the stomach. This state of suffering may last from half-an-hour to three or four hours, and then cease to return after some days or months or years.

In the urine the presence of oxalate of lime may be suspected when sudden changes in the quantity made in twenty-four hours are observed.

A slightly dyspeptic gentleman was passing urine giving a thick deposit of urates only on cooling. The amount made in twenty-four hours was twenty-nine ounces, specific gravity 1023·8. The following day, without any change of diet, and without drinking more fluid, and without medicine of any kind, he passed fifty-four ounces, specific gravity 1018·1, and on examination myriads of octahedral crystals were found to be present.

Usually an increased urgency and frequency of making water accompanies this increased flow, and there is a general feeling of irritability of the nervous system, exaggerating

external and internal annoyances to a degree far beyond that to which they would rise if no dyspepsia existed.

W. S., aged 64, had all his life been dyspeptic. For twelve years he had had dry and moist eczema. For seven or eight years he has had sleepless nights; at times so excessively nervous he could not go to bed. Has had violent pains on the top of the head, and spasms of the stomach, lasting half-an-hour or an hour, relieved by an escape of wind. For the last two years he has had frequent calls to pass water at times. Has never had a distinct attack of gout, but frequently has flying pains in the joints. Without known cause, he frequently, for some hours, passes large quantities of water, with increased frequency in the morning, but not in the evening. For example:—

On Feb. 13 he passed—	ozs.	On Feb. 14 he passed—	ozs.
At 2 a.m.	4	At 7 a.m.	8
3.30	5	8 breakfast.	
7.30	6	10	2
8.30	6	2 p.m.	4
10 breakfast.		Dinner.	
12 noon	7	5.30	4
2 p.m.	4	8	$2\frac{1}{2}$
4.15	4	12	$2\frac{1}{2}$
6 dinner.			—
8	5		26 sp. gr. 1026
12 night	4		
	—		
	45 sp. gr. 1015		

In the water passed on the 13th I found plenty of octahedral crystals; in that of the 14th I found free uric acid and urates. There was no other disease detectable.

On the Consequences of the Oxalic Diathesis.

The formation of an oxalate-of-lime calculus in the kidney or bladder is the secondary disease which the oxalic diathesis produces. But for this mechanical complaint the chemical disorder would be of little or no importance at all. Hence the great object of detecting oxalate of lime in the urine

is to prevent the formation of mulberry stone in the urinary organs.

In my paper in the 26th vol. of the 'Transactions' of the Medico-Chirurgical Society, I have stated that out of 450 distinct deposits forming calculi, 135 times uric acid was found alone or mixed with other substances, and 163 times oxalate of lime occurred either alone or mixed with other deposits. In other words, the greater degree of acidity which is marked by uric-acid crystals occurred rather less often than the lesser degree of acidity which led to the formation of the oxalic acid diathesis. In other collections the greater degree of acidity appears to have more frequently caused the formation of the calculi. From the analysis of many collections, Dr. Prout says, p. 590, "If a mulberry stone had not been formed and detained in the bladder, two persons out of about nine who suffer from calculus would not have been troubled with that affection." As he previously said that six out of nine had a nucleus of uric acid (or urates), it follows that imperfect oxidation to a greater or less degree gives rise to no less than eight out of nine cases of stone.

With regard to the mechanical effects of mulberry stone, they scarcely differ from those produced by uric acid. Usually the mulberry stone is rougher and harder than all other stones; and hence the roughness is more apt to cause blood by hurting the kidney or bladder, and greater mechanical force is required to crush the stone, and the fragments are sharper and harder than those of any other kind of stone.

In addition to the mechanical diseases of stone in the kidney, ureter, or bladder, the oxalic acid diathesis, or in other words, that degree of oxidation which causes the formation of oxalic acid instead of carbonic acid, may perhaps hereafter be found to produce secondary chemical disorders.

Thus in diseases which are accompanied with great difficulty of breathing or in extreme states of debility, as perhaps in asthma or at the end of different fevers, oxalic acid may accumulate in the blood or in the textures, and either alone or with the help of carbonic oxide gas produce a

state of narcotic poisoning not to be distinguished in its phenomena from the effects of a fatal dose of morphia.

In the 'Transactions' of the Medico-Chirurgical Society for 1849, p. 171, Dr. Garrod records a case of Bright's disease with effusion in the chest and abdomen, in which oxalate of lime was found in the blood; the patient became senseless eight hours before death, possibly, however, from urea in the textures.

On the Treatment of the Oxalic Diathesis.

The treatment of the oxalic diathesis and the treatment of oxalate of lime in the urine are almost, though not altogether founded on the same indications. The cure of the oxalic diathesis is to be obtained by promoting oxidation in the body. In this respect this disease and diabetes have the closest possible resemblance. The best treatment for flatulent dyspepsia is the best treatment for diabetes. I must refer you, then, to all I have said on the treatment of diabetes for the fullest information on the treatment of the oxalic diathesis. I might sum all up, however, in four words—meat in moderation and weak spirit; nevertheless, a diet as rigid as in diabetes need not be insisted on in this complaint; because it is often so slight an aberration from health that the functions of the body are scarcely interfered with, and if it were not for the formation of oxalate of lime it might often be altogether neglected.

Hence the treatment of oxalate of lime becomes of more importance than the treatment of the oxalic acid diathesis. Two methods may be simultaneously carried out—first, the amount of lime passing through the body may be lessened, and secondly, the formation of the octahedral crystals may be stopped.

The effect of diminishing the amount of lime taken into the body by the drinking water may be seen from what results when the quantity of lime in the urine is increased, either by adding it after the water is made, or by giving lime salts as medicine. The following experiments among many

others that I might give, are quite sufficient to show the importance of giving rain or distilled water when much oxalate of lime is found in the urine :—

250 c.c. of fresh nearly neutral urine were divided into five equal parts.

To the first part nothing was added; it was examined twenty-one hours afterwards, and gave no octahedral crystals.

To the 2nd. One drop of chloride of calcium solution, sp. gr. 1146, was added; octahedra were found.

To the 3rd. Two drops of ditto; octahedra.

To the 4th. Three drops of ditto; octahedra.

To the 5th. An excess; many octahedra.

Seven other experiments were made with different healthy urines.

Two equal portions of the same urine were taken, and chloride of calcium was added freely to one after it was passed.

Experiment 1.—The urine without chloride of calcium contained very few octahedral crystals; with chloride of calcium many small octahedra.

Experiment 2.—The urine without chloride of calcium contained no oxalate; with chloride of calcium plenty of octahedral crystals.

Experiment 3.—The urine without chloride of calcium contained urates and only a few octahedra; with chloride of calcium a large amount of octahedra, large crystals.

Experiment 4.—The urine without chloride of calcium contained no octahedra; with chloride of calcium exceedingly small crystals, not quite distinct as octahedra.

Experiment 5.—The urine without chloride of calcium contained very few and very small octahedra; with chloride of calcium plenty of octahedra.

Experiment 6.—Doubtful increase of oxalate by adding chloride of calcium.

Experiment 7.—Doubtful increase.

If lime-water or acetate of lime or carbonate of lime are

given as medicine, oxalate of lime may be expected in excess in the urine.

C. W., aged 30, was admitted with chronic rheumatism into St. George's Hospital, July 30. The urine was acid and perfectly natural, excepting that occasionally a little bladder epithelium was seen. Forty-five grains of acetate of lime dissolved in water were given thrice daily; in four days oxalate of lime crystals in plenty were found in the urine.

L. B., aged 26, admitted with slight rheumatism. The urine was acid and perfectly natural, except that it contained a quantity of pus cells, the result of gonorrhœa. Thirty grains of acetate of lime were given thrice daily for two days, and then forty-five grains for two more days, when much oxalate was found in the urine.

Distilled water or rain water are therefore likely to be useful when octahedral crystals are found in the urine. Even the removal of some of the lime from the drinking water by boiling it well, and then filtering it, or, better still, by adding a little carbonate of soda before boiling, may be of use in stopping the rapid formation of oxalate-of-lime gravel in the urine.

It is quite impossible to stop all lime from going in or coming out of the body; and, therefore, by the anti-lime treatment, only a partial good can be done, and other methods of stopping the crystallization must be adopted, or still better, the oxalic acid diathesis must be removed.

The second method of treating the oxalate of lime deposit in the urine consists in stopping the formation of the crystals. Removing the oxalic acid diathesis would stop the crystallization as surely as it would be effected if no lime could be allowed to pass out of the body; and though both these methods may be of use, a still more immediate effect on the crystallization may be obtained by the mineral acid treatment.

Dr. Prout first ordered a mixture of one part nitric and two parts hydrochloric acid. This is called nitro-muriatic

acid. It varies in composition according to the temperature at which the acids are mixed and kept, and according to the time they remain mixed before they are used. Sometimes it is a mixture of nitric and hydrochloric acid, or it may contain chlorohyponitric and chloronitrous acid, or even hyponitrous acid and chlorine. It is, no doubt, possible that a mixture of these substances may be more beneficial as a medicine than any one of them used separately; and if this can be proved to be true, such a mixture should be used; but the progress of our knowledge of remedies depends on the use of each substance separately, in order that the greatest possible clearness may be obtained as to the effect of each remedy; and, as it is by no means proved that so-called nitro-hydrochloric acid is superior in any respect to the mineral acids taken singly, I consider that an advance in clearness of intention, if not in power of treatment, may be obtained by using each acid separately, according to the properties which each must be considered or may be found to possess.

And first regarding hydrochloric acid. As this is more especially the acid of the gastric juice, it seems reasonable that it should be prescribed, more particularly when there is feeble digestive power; after long illnesses, when animal food begins again to agree, it should be taken almost immediately before each meal of animal food. Thus the greatest immediate use can be got out of hydrochloric acid.

Secondly, regarding nitric acid. This acid was at one time strongly recommended as a substitute for mercury in syphilis and in the liver diseases of India. Generally, it may be considered to promote secretion and perhaps oxidation; and with this intention it should be given so as to be absorbed before food enters into the stomach. If taken one hour or two hours before meals on an empty stomach, the nitric acid acts on the system and not on the food.

Thirdly, sulphuric acid has been always used as an astringent to stop perspiration, to stop hæmorrhage, to stop diarrhœa. It may be, therefore, regarded as the opposite of nitric acid

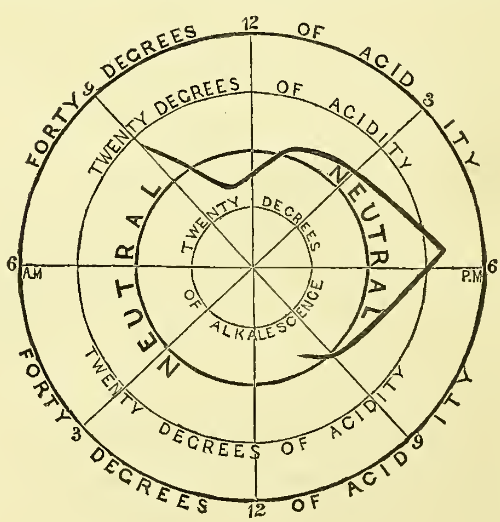
in its action on the system; and to obtain the greatest action it also should be given in time to admit of its absorption before food is eaten.

Thus, then, rightly used, hydrochloric acid promotes digestion, nitric acid secretion, sulphuric acid constriction.

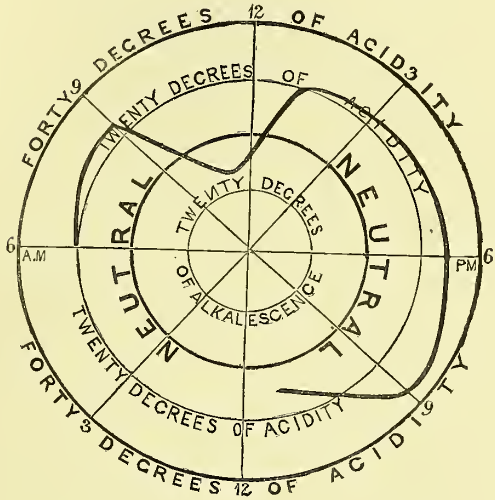
In addition to these special actions, there is a direct local action of these substances on the stomach. When used in small quantities, with care, they all probably render the stomach less irritable than it otherwise would be; but if the dose of any of them be too strong, it probably increases the sensitiveness of the mucous membrane, and may cause violent pain and spasm, increased chemical action producing altered mechanical and chemical actions in the mucous membrane of the stomach.

All these acids also have a distinct action on the urine. Although there is as yet no positive proof that dilute mineral acids increase the acidity of the urine at all to the same degree that dilute vegetable acids can do—for example:

Variation of the acidity of the urine during the day when three drachms of dilute sulphuric acid, sp. gr. 1·1077, *are taken in water.*



Variation of the acidity of the urine during the day when eighty-four grains of tartaric acid are taken in water.



yet, if the amount of sulphates, for example, in the whole quantity of water passed in twenty-four hours for three successive days when no sulphuric acid is taken is compared with the amount of sulphates in the whole quantity of water passed in twenty-four hours for the three succeeding days when sulphuric acid is taken, it is certain that dilute sulphuric acid taken in very large quantity does pass off combined or uncombined in the urine. The third day after half an ounce of dilute sulphuric acid, specific gravity 1·1084, had been taken daily, 43 ounces of urine were passed of specific gravity 1025·4. 12·95 grains of sulphate of baryta were precipitated from 1000 grains of this urine; when no acid was taken 42 ounces of urine were passed of specific gravity 1023·4. These gave 9·19 grains of sulphate of baryta per 1000 grains of urine.

All the mineral acids lessen the tendency of the oxalate of lime to form crystals in the urine. If two equal portions of urine are taken, and the minutest quantity of mineral acid is added to one portion, whilst the other is kept for comparison without acid, oxalate of lime may be found in the urine to

which no acid has been added, whilst in the other no crystals will form. The same action may occur when these acids are taken as medicine, and with nitric acid there is the additional recommendation that the oxalic acid diathesis itself may, by the promotion of oxidation, be lessened or, with perseverance, removed.

LECTURE VI.

DISEASES OF SUBOXIDATION.—ON URIC-ACID GRAVEL.

In this and in the following lecture on gout I intend more particularly to bring before you the mechanical and mechanico-chemical consequences of the uric acid diathesis—that is, of excess of acidity.

The relationship that exists between chemical disease and mechanical disease cannot be more clearly set forth than in the production of gravel or stone from errors in the chemistry of the body.

I have dwelt only on chemical disease in the two lectures on diabetes and acidity, and I have given you a particular instance of chemical error and of its mechanical consequence, or secondary disease, in the last lecture on the oxalic diathesis; I intend now to occupy your attention with the mechanical consequence of acidity in general; and I shall have occasion to show you that this secondary mechanical disease may produce tertiary chemical derangements vastly greater than the original primary chemical wrong, out of which the secondary mechanical disease arose.

I have already explained to you the causes of acidity. I have now more particularly to dwell upon one of the results of that acidity; in short, on the nature of the gravel that is caused by excess of acidity, the means of detecting it, the symptoms it produces, its consequences or complications, and its treatment.

On the Nature of the Gravel that is caused by Over-acidity.

Generally speaking, it may be said that all the albuminous substances of vegetable or animal food, before they are thrown out of the body, pass through the stage of uric acid. A particle of albumen absorbed into the blood from the food may become part of an organ and serve the purposes of life, and

then undergoing change become resolved into uric acid, then into urea and oxalic acid, and finally into urea, carbonic acid, and water; or the particle of albumen may go through a shorter circuit, and without becoming part of any organ or texture it may be transformed into uric acid, and ultimately pass off as urea, carbonic acid, and water.

Thus uric acid, like sugar, may come from two sources—first from the food, and secondly from the textures; and as sugar is one of the results of healthy chemical action, through which, generally speaking, every particle of starch must pass, so uric acid is one of the substances through which each particle of albumen in health passes before it is thrown out of the body. When more food is taken into the blood than is wanted for the muscles, nerves, and textures generally, the excess is thrown out in a more or less perfectly oxidized form by the kidneys, skin, and lungs; it may be as uric acid, or if further changed as urea, oxalic acid, and water; or if burnt, as far as possible, as urea, carbonic acid, and water; or different portions of the albumen may be thrown out in all these different states at the same time.

The excess of uric acid in the urine of those who have just taken an excess of albuminous food, whether animal or vegetable, is very easy of proof.

The quantity of uric acid in the urine I found to vary (see 'Philosophical Transactions,' Part II., 1849, p. 235)—

			Sp. gr.
Before food (mixed diet) from	0·048	grains per 1000 grains of urine	1026·3
to	0·17	„	1023·1
After food it varied from	0·39	„	1021·0
to	0·92	„	1031·1
On vegetable food—			
Before food . . .	0·049	„	1024·0
After food . . .	0·636	„	1026·2
On animal food—			
Before food . . .	0·049	„	1024·8
After food . . .	0·77	„	1029·9
After three days of animal food only the highest amount was . .	1·022	„	1027·8
After three days of vegetable food only the highest amount was . . .	1·010	„	1025·6

The second source of uric acid is in the muscles, nerves, and other textures of the body. Wherever albuminous substances exist—that is, in each portion of the body—integration is continually balanced by disintegration, and one of the products of this disintegration of albumen is uric acid, which returns into the blood, and, more or less oxidized, passes off by the kidneys, and is found in the urine when no albuminous food at all has been taken for many days.

Derived from either source, uric acid exists in combination with alkalies dissolved in a more or less alkaline fluid in the blood. In the cells of the kidneys and elsewhere a process of oxidation occurs; other acids are produced, and the alkaline urates are made into more acid urates, which pass out of the kidneys to the amount of six to ten grains of uric acid daily dissolved in an acid fluid which is continually varying in acidity. Hence the composition of the urates in the urine is continually differing at different times.

In a paper in the 'Journal of the Chemical Society' for 1862, vol. xv., p. 201, I have shown that in health potass, soda, and ammonia are all combined with uric acid in varying quantities, and these mixed urates constitute the ordinary granular amorphous deposit which is soluble in the warm urine. In three analyses I find—

	First Analysis.	Second Analysis.	Third Analysis.
Uric acid . .	94·36	91·06	92·11
Potassium . .	3·15	3·78	5·06
Ammonium . .	1·36	3·36	1·61
Sodium . . .	1·11	1·87	1·20

These acid urates are sometimes combined with uric acid, forming still more acid urates, corresponding to quadoxalates, from which a portion of the uric acid is set free even by washing the amorphous sediment with water. If any acid acts on the acid urates they are decomposed, and uric acid is set free more or less quickly, according to the strength and temperature at which the acid acts. Thus, if in the cells of the kidney by oxidation mineral, vegetable, or fatty acids are produced, the urates are decomposed either in the tubes of the kidney, the pelvis of the kidney, the ureter, or in the

bladder. Hence any acid whatever except the acid of extreme oxidation—carbonic acid—may give rise to uric-acid gravel. Whatever the acid that may be taken in excess in the food, or whatever the acid that may be thrown on the kidney by inaction of the skin, or whatever the acid that may be produced in the stomach or in the kidney itself, if it decomposes the urates it may give rise to uric-acid gravel. Acid phosphate of soda is not able to set free uric acid from the urates: free acid must be present; and hence free uric acid is the most delicate test of other free acids in the urine.

On the Means of Detecting the Uric-Acid Gravel.

In contradistinction to white or phosphatic gravel, and to black or oxalic gravel, this may be called red or uric gravel; but colour, though striking, is apt to mislead. Pure uric acid is as perfectly white as phosphate or oxalate of lime, and, though uric acid attracts to itself the colouring matter of the urine, and so becomes reddish-yellow, yet there may be next to no colour to attract, and so the gravel may remain white, and then chemical reactions or microscopical appearances can alone determine the nature of the deposit.

The chemical test for uric acid is very characteristic. The smallest portion of sand or gravel heated with nitric acid at a gentle heat is immediately oxidized. Among the products is murexan, which gives, with ammonia, the richest purple murexide, and by this reaction uric acid may be always known. Thus, however, you cannot determine whether the uric acid is free or in combination. Chemically this may be partially determined by fully oxidizing the sand or gravel; if, on combustion, an ash remains, the uric acid is combined with some fixed base; but ammonia is volatile, and thus the surest method of determining whether the uric acid is combined or free is to observe the deposit as it passes in the urine with the microscope. Moreover, thus a single crystal of uric acid can be recognized; a quantity much too small to be tested chemically can be determined microscopically with certainty. Of course, errors of observation may arise, but the practised

eye will learn to recognize the various forms of uric-acid crystals, and possibly the peculiarity of form may lead to a knowledge either of the acid which set the uric acid free or of the composition of the fluid in which the uric acid was set free.

Having determined that free uric acid is present, it is of importance to know how soon the crystals form after the urine is secreted by the kidney—whether they form in or out of the body. For this the urine should be passed into a bottle or glass and examined immediately, and if no crystals are then seen, every twelve hours a fresh examination should be made; and thus the amount of acid which is acting on the urates may be estimated and counteracted.

On the Symptoms produced by Gravel.

When the red sand only forms after the urine is passed, it causes no symptoms whatever; but the acid or acids in the urine, which after a time liberate the uric acid, these may produce irritability of the bladder or of the urethra. Over-acid urine sometimes causes excessive frequency and urgency of making water. The mucous membrane may be made so irritable that inflammation and all the symptoms and appearances of violent gonorrhœa may be produced; or the muscular texture of the urethra may be irritated, and spasm ending in spasmodic stricture may occur.

These chemical irritations do not, strictly speaking, proceed from the red sand; they come from the cause of the red sand; but they are necessary accompaniments of the mechanical irritations which the gravel occasions; and these we have now to consider.

As the gravel may form in the bladder, the ureter, or the kidney, so the mechanical irritations may begin in these different places, and the symptoms will vary according to the part that is irritated.

We will take the mechanical symptoms produced in the kidney first, although the formation of gravel in the kidney is a sign of the greatest degree of acidity, because the urine

only remains a few seconds in the kidney, whilst it may remain some hours in the bladder. The acid in the kidney must be much stronger, in order to set free the uric acid, than it need be in the bladder to produce the same effect, because less power in longer time produces the same result as a greater degree of acidity in a shorter time.

As long as the gravel is small, and lies unmoved in the pelvis of the kidney, no symptoms occur. During rest no microscopical or chemical signs or general symptoms show the presence of a foreign body in the kidney; but if sufficiently rough motion is made, then the gravel moves in the kidney, and, slightly scratching the surface, blood becomes mixed with the urine. The injury to the pelvis of the kidney may be far short of causing pain or visible blood; there may be so little, that chemical tests for albumen may give no reaction of that substance; but yet the microscope may show distinctly a very few blood-globules. These may come with motion and cease with rest. With much motion, much blood will come, and be visible in quantity in the urine; and this may occur without the least pain. So that I often ask my patient with hæmaturia from this cause whether he would know that anything was wrong if he were blind, and the answer is usually positively no.

Gradually as the gravel increases in size in the kidney, slighter motion brings blood, and pain, and uneasiness in the loin. Distension of the colon, with flatulence, when it presses on the kidney, causes considerable pain.

If the gravel does not pass into the ureter, very little pain arises until the increase of size leads to pressure on the kidney and absorption of structure. I have seen cases in which I have no doubt that calculi have been in the kidney for very many years. In proof of this I may mention, from among many others, the following cases of seventeen, twenty, and probably of fifty years' duration.

A needlewoman, aged 47, was admitted into St. George's, having had occasional attacks of pain in the left side with blood in the urine for seventeen years. On deep pressure in front, below the left hypochondriac region, a hard oval tumour

could be distinctly felt. The urine was acid; specific gravity 1015; contained blood and pus cells, plenty of vibrios, but no crystals of uric acid nor oxalate of lime.

A clergyman, aged 41, consulted me for the appearance of blood in the urine, which he had seen for twenty years. The urine was thick from urates, acid to test-paper, and contained a few blood-globules. He had been obliged to give up hunting because it brought on blood in the water. I saw him occasionally for some years, and always with the same appearances in the urine after exercise.

An officer, aged 61, told me that for twenty-four years he had been subject to attacks of pain in the left lumbar region, with blood in the urine. Warm bath and rest always gave relief to the pain and stopped the blood. He had had innumerable renal attacks, without passing any stone, but was able to travel each year on the Continent without much inconvenience.

A carpenter, aged 61, consulted me for a continual pain in the left kidney. Sometimes a dead heavy pain, at other times most acute during work or when walking. He is then obliged to throw himself down on his back and side until the pain passes off. If detained even for a few minutes after his usual meal-times the pain is often most acute. Any excitement will "either increase or subdue it." I found that the urine had the slightest trace of albumen and most distinct evidence of blood-globules. There was no pus, no increase of mucus, and no crystals of any kind. The urine was acid. He said that when eleven years old the pain first came on very suddenly with blood in the urine. The pain had never since entirely left him, and he has very frequently seen blood in the water. Latterly the pain had become more constant and more severe. For fifty years through an active life this man had probably had a stone in the kidney.

The symptoms produced by gravel in the ureter are much more severe than those produced by gravel in the kidney. The instant the gravel or stone produces mechanical pressure violent pain comes on. The funnel form of the commencement of the ureter allows the gravel easily to escape a short

distance from the kidney; and hence after some sudden jerk or even a turn in bed the pain begins suddenly and is referred to the kidney itself. Through reflex action, vomiting soon follows. According to the size of the gravel or stone and the size of the ureter, the narrow passage is more or less quickly passed, and with a slight obstruction at the still less elastic entrance into the bladder the mechanical impediment is over, and the symptoms cease.

The symptoms produced by gravel or small stone in the bladder correspond with those produced in the kidney. At first there are no symptoms at all; violent exercise may produce microscopic appearance of blood, but until the gravel tries to escape, or is thrown by contraction of the muscular texture on the neck of the bladder, no pain is felt. Gradually as the stone increases, or the bladder becomes irritated and wants to contract frequently, blood becomes visible, and pain on motion and on emptying the water becomes severe. This pain is referred to the extremity of the nerves at the end of the penis. The flow of urine may be momentarily broken by the gravel or stone stopping the passage. If the stone is small enough or the urethra large enough the foreign body escapes into the tube, and in a longer or shorter time it is driven out.

Although gravel may stop in the urethra and gradually increase there until mechanically removed, yet it is very unlikely that it should begin to form there. If the crystallization commenced there, the passing urine would rapidly wash the crystals away before they caused any symptoms; so that the urethra does not thus suffer primarily from wrong chemistry. But the peripheral pain of the glans penis, and the scalding of the urethra from the acid urine, and the mechanical injury which the sharp fragments of acid stones occasionally produce in the urethra after lithotrity, these all show that even the urethra does suffer from mechanical secondary disorders arising from primary chemical complaints.

On the Consequences Produced by Gravel.

The tertiary diseases which arise from gravel or stone are chemical or mechanical. We will for clearness divide them according to their birthplaces.

1st. The kidney often becomes inflamed from the mechanical irritation of the pelvis. Pyelitis is set up; pus forms and escapes continually for years without pain, or if it have not a free exit it is passed intermittently, with more or less violent pain, sometimes almost causing as much suffering as a renal calculus makes when passing. In these cases the pressure on the pelvis of the kidney being the same as on the obstruction, the pyramids are changed into calices, and ultimately the whole kidney is absorbed, and becomes lost in the abscess.

J. C., aged 32, was admitted into St. George's Hospital in October, 1843, for acute double pleurisy, with effusion. He died comatose on February 11, 1844. The right kidney was healthy; the pelvis, infundibula, and calices of the left kidney were very much dilated, and filled with a thick fluid mixed with gravel and sand. The dilatation depended upon a stricture of the ureter, which existed two inches from the pelvis of the kidney. The ureter was still pervious, but a pig's bristle was the only thing that could be passed through the stricture, which was not more than two lines in length. The other portion of the ureter presented nothing remarkable beyond a slight discoloration. The parts in the neighbourhood of the stricture of the ureter were not thickened.

2nd. The stone or gravel lodges in the ureter, and there produces mechanical and then chemical symptoms.

A gentleman, aged 55, was seized with pain in the loin and vomiting on March 23, 1850. The urine was very scanty until the morning of the 26th, when he ceased to make any. The catheter was passed on the 27th, and no urine was found in the bladder. On the 28th he had some delirium, and much increased vomiting. On April 3 there was great drowsiness, with delirium and hiccup; at 11 p.m. still no urine was in the bladder. On the 4th, at 4 a.m., after very great pain, he passed two pints of clear urine and a very small stone; it

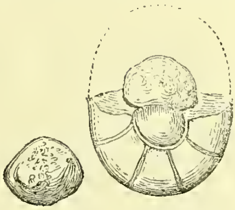
consisted of oxalate of lime, and did not weigh half one grain. For nine whole days no water whatever was passed, and for three days previously only a very small quantity of urine was made. On April 12 the patient was in his usual good health.

On November 23, 1844, I saw a gentleman, aged 54, with a renal attack of three weeks' duration. There was much pain in pressing over the region of the left kidney either before or behind, and there was more fulness in passing the hand over the left lumbar region than over the right. The urine was alkaline, and contained blood. In December the attack gradually went off, and on the 20th he passed a calculus consisting of phosphates and urates; it was the size of a small bean. In three days he appeared quite well. On the 24th he had some pain in the region of the left kidney. On the 27th, pulse 110, jerking; face flushed; skin cold; unable to sleep; tongue brown; urine thick from pus-globules and alkaline. 28th, pulse feeble, intermitting; tongue dry; brown; hiccup; distension of abdomen; very little urine secreted. He sank the following morning. There was general peritonitis, and a large abscess in the cellular tissue around the left kidney extended up to the diaphragm. On trying to remove the kidney with the ureter, it parted an inch and a half below the pelvis, though very little force was used. The ureter to this point was dilated so as to admit the little finger. The lower end of the ureter was not dilated. The pelvis and calices of the left kidney were much dilated, and contained gravel.

3rd. The stone may stop in the bladder, and there also produce mechanical and chemical symptoms. Slight rupture of vessels and consequent hæmorrhage on motion, and pain in the glans when the stone is pressed on the neck of the bladder: these are the two chief signs of cystic calculus.

Sometimes the hæmorrhage is enormous. On December 29, 1850, I saw a gentleman, aged 68, who had passed large fragments of uric-acid calculus from his bladder. Eight of these fragments, and a large piece the size of a pea, he had collected and put together, forming a stone nearly as large as the first joint of an ordinary thumb. Two or three fragments only were wanting to make the stone perfect. He began to pass a

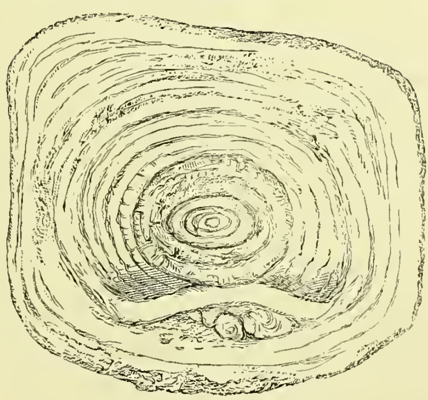
little blood without pain on the 28th; at 8 a.m. on the morning of the 29th he passed very bloody water. I saw him about twelve hours afterwards. The bladder was distended, forming a perceptible tumour in the abdomen. On the 30th there was a very little bloody urine discharged, but the tumour in the abdomen was less distinct. There were no urgent symptoms, and as he had on a previous occasion suffered in the same way, and no instrument was then passed, I let him alone. On June 31, clots and urine came away, and the following day he made clear urine.



Nucleus. Whole Stone.

The following extreme case of mechanico-chemical disease occurred to Mr. Prescott Hewett:—

R. R., 17 years of age, was admitted into St. George's Hospital for gravel and irritation in the bladder, from which he had suffered as long as he could remember. The urine was alkaline and purulent; on examination by the rectum a large rough stone was felt pressing backwards, and on pushing it upwards it was felt in the abdomen. The stone was so large that it was proposed to dissolve off the phosphates by hydrochloric-acid injections previous to any mechanical operation; but before anything was done, the patient after a week of fever died. Three externally phosphatic stones were found in the bladder: one weighed 120 grains, another 115 grains, and the third 5 ounces 120 grains. The drawing represents the size and appearance of the large stone.



The history of the case, as it is recorded on this stone, is very unusual. At first acidity caused a small stone to form in the kidney, where it remained increasing by different degrees of acidity for some time, after which it was passed into the bladder. There the acidity continued very uniformly for as long a time as the stone had been in the kidney. Then it set up inflammation of the bladder, and the stone by nearly one-fifth of its surface became adherent to the bladder, the urine became alkaline, and the phosphates were deposited wherever the stone was not attached. This lasted for a considerable time, the phosphates being mixed with urates in variable quantities. Then the adherent part separated, and an irregular stone one-fifth depressed and four-fifths oval was free in the bladder. After this a more phosphatic state was produced, and when this had lasted for a short time two other small stones probably passed from the kidney, and lodged themselves in the depressed part of the large stone, and these were soon united by fresh phosphatic deposit, which went on increasing the calculus until the death of the patient, when the depression was entirely obliterated.

This stone by mechanical pressure had caused ulceration of the bladder, and a circumscribed abscess had been formed in the peritoneum the size of a cricket-ball, which opened into the bladder; another ulcerated opening led into the cavity of the peritoneum, which was inflamed throughout, the intestines being glued together by purulent fluid. The bladder itself was thickened, and the mucous membrane coated with phosphates.

4th. The urethra is the rarest birthplace for mechanical or chemical tertiary calculous disease. Occasionally a piece of gravel obstructs the passage, or inflammation of the bladder spreads to the urethra, and the angular fragments after lithotrity excite much inflammation, and have even been known mechanically to cut through the tube, and blocking up the natural passage, to cause extravasation of urine and death. But these are rare accidents, and belong more to the surgeon than to the physician; still, if time permitted, such cases would furnish me with the very best illustrations of the rela-

tionship that exists between mechanical and chemical diseases, showing how, out of the motion of masses of matter, molecular motions arise in consequence of that correlation of force in the body which constitutes the subject of these lectures.

On the Treatment of Uric-Acid Gravel.

In the treatment of every kind of gravel the first question is regarding its solubility. The solution of uric-acid gravel in any alkaline fluid that can be borne in contact with the mucous membrane of the urinary organs is scarcely possible. It can hardly be doubted that uric acid in a fine state of division as powder could be dissolved, but the problem is to dissolve uric acid in a more or less massive state. The mechanical force of cohesion of the crystalline particles as well as the chemical insolubility of each crystal has to be overcome. And notwithstanding the appearance on the surface of some uric-acid calculi, and notwithstanding the supposed disappearance of calculi that have been considered to be in the urinary organs, and notwithstanding I have made numberless experiments, in the body and out of the body, to find a solvent for the stone in the kidneys or in the bladder, yet at present the state of aggregation of masses of uric acid cannot be overcome chemically. Acid gravel has not been dissolved in the kidneys or bladder by medicines; still my friend Dr. Roberts, of Manchester, is confident of success, more so than I am.

Until the gravel comes away or is removed two chief indications for practice exist. Firstly, to prevent it from hurting the mucous membrane, and secondly, to stop its enlargement.

Pain and blood are the evidences of hurt to the mucous membrane. Hence, any amount of exercise or of motion may be taken, provided it does not cause pain or blood. The amount of pain may be taken as the measure of the risk of inflammation, and the amount of blood may also be taken as the measure of the mechanical hurt to the kidney, and of the loss of strength which results from hæmorrhage. Both pain and blood may be prevented or temporarily removed by rest; but long-continued perfect rest would in most people soon

injure the general health. So that the mean must be found by trials, the problem being to keep up the general health by exercise, but to avoid by rest inflammation or hæmorrhage—that is, chemical or mechanical injury.

The second indication is to stop the growth of the stone. In other words, to prevent fresh acidity; for thus the gravel is kept so small as to admit of perfect cure by the escape of the mechanical mass through the urinary organs. The means of preventing acidity have been already brought before you. Here I shall say only a few words on the good of dilution, which not only delays the precipitation of the uric acid, but helps to wash out the gravel or stone. The best diluent is some alkaline mineral water, as Vichy, or Fachingen, or Seltzer water, taken not only with the food, but two hours before each meal. When there is no acidity, soft spring water night and morning is the best diluent.

This brings me now to the treatment of the passage of gravel or stone from the kidneys or bladder. The chief objects to be obtained are, first, to relieve pain; and secondly, to promote the passage of the calculus.

The pain is most rapidly removed by chloroform or ether inhalation. This, with care, may be continued for hours. The slightest unconsciousness is all that is necessary; but this must be kept up, for on the return of consciousness the pain is again felt.

The second remedy is the hot-bath at the temperature of 100° F. continued for hours, unless it causes faintness. "Four hours' bath and then two hours' warm blankets; then three and a-half hours' bath and three hours' warm blankets; continue in this manner, gradually prolonging the rest and shortening the bath. Nothing weakens like pain." Or any hot applications may be used when the bath cannot be taken.

The third remedy for pain is opium, externally or internally.

Externally, it may be used as a fomentation in any quantity; as laudanum or solution of morphia poured on a poultice, or with one-eighth to one-sixteenth of chloroform on spongio piline. Internally, half a grain or more of acetate of morphia in solution may be injected into the loin; within a few minutes

it will act potently on the pain; or opium, or any of its preparations, may be given by mouth freely, and the severity of the pain renders the system tolerant of large doses; but the ill effects of the sedative in causing inaction of the liver and constipation are very evident when the pain ceases. Half a grain or even two-thirds of a grain of morphia may be given by the mouth, and repeated in four or six hours, if the pain lasts; or thirty drops of laudanum may be taken, and repeated in two or three hours. For the relief of the suffering it is best that the aperient should be taken at the same time as the opiates, the action of the aperient counterbalancing the action of the narcotic on the bowels. Calomel in full aperient doses, as it stops sickness, may be given with the opium if there is great constipation, or if there is great intolerance of narcotics.

Secondly, the passage of the calculus is probably made easier by all the means that relieve pain. When the spasm is relaxed by chloroform and opium, or by the warm bath, or by fomentations, the escape of the calculus is made more easy. Still, the pressure of the urine behind the obstruction is the great motive power in the passage of the gravel or stone. This force comes into action only when the obstruction is more or less complete, and then the pressure of the fluid is the same on the structure of the kidney as on the obstruction; and thus the secretion of urine is lessened, and the pressure more and more slowly reaches its maximum. Diluents may early in the attack be of use in increasing the pressure; but after the symptoms of suppression of urine occur, they are of less use in this respect, and when urinous poisoning comes on vomiting and purging give relief by removing some of the poison. Usually, without emetics or aperients, sufficient, sometimes excessive, evacuation takes place; and if this tertiary chemical poisoning does not bring the heart to rest, the obstruction of the ureter may be removed by the continued pressure, and then, the circulation through the kidney being free, the blood is rapidly purified, and a chemical disease (urinous poisoning) far more dangerous than the original chemical complaint (acidity) rapidly passes away.

When the obstruction cannot be removed, not only does the

pressure of the secreted urine stop the purification of the blood by stopping secretion, but the urine that has been poured out must, by diffusion, pass back into the blood. When the blood is urinous, diffusion must carry the poison to every part of the textures, even into those parts where no vessels exist —the cornea, the crystalline lens, the cartilages, and, perhaps, even into the nails and the hair. The uric acid, oxalic acid, and urea poison the nerves and muscles and blood-vessels and other textures, and render them incapable of carrying on the actions of nutrition and oxidation.

When the gravel passes into the bladder, usually little or no treatment is requisite. After a longer or shorter delay the stone is forced into the urethra, and ultimately is driven out; but whilst it remains the same objects are still to be kept in view—first, to promote the escape of the stone; secondly, to prevent its growth; and, thirdly, to keep the bladder from harm.

Free dilution and alkaline remedies best fulfil the first two objects; whilst the last is chiefly to be gained by rest. Inasmuch as the bladder is nearer the external orifice than the kidney, two or three other remedies are possible.

First. There is great surgical authority for occasionally passing a catheter when a small stone is suspected to be in the bladder. If there be no stricture, it is not easy to see how this should help the passage of the stone more than passing a probang before food would make swallowing easier.

A gentleman came to me one morning, and from the microscopic blood in the urine and the pain in making it, whilst his general health was robust, I considered a stone had formed in the bladder. I went with him to a surgeon, who sounded him, and said "There may be a stone, but I cannot find it." The following morning the patient brought me the stone, which he had voided in the night. To him, and to his surgeon, it was beyond all doubt that the passing the sound made the stone come away.

Secondly. The Astley Cooper forceps, by which a small stone may be removed whole through the urethra; and the lithotrite, by which a stone may be removed in pieces; and,

still more, lithotomy, by which the foreign body is removed whole through an artificial opening, are mechanical proceedings belonging to the surgeon and not to the physician.

Thirdly. There is yet another method of cure, so far beyond all other methods in its philosophy, its safety, and its freedom from suffering, that success, though still postponed, must ultimately be attained. This is the dissolving the gravel in the bladder. There is no difficulty whatever, excepting want of patience and chemical knowledge, that hinders the solution of phosphates in dilute acid. A stream of diluted lactic or hydrochloric acid, made so weak as not to irritate the bladder, and passed at the temperature of 100° F., must dissolve any phosphatic gravel or stone or outer layer of stone, provided only that the current be continued long enough.

A warm stream of very diluted lithia or soda should dissolve any urates and attack uric acid. But gravel and stone vary very much in density, that is, in compactness of aggregation, and some uric-acid gravel is so hard that it is vain to expect that any stream of water or of alkaline water will have any effect in any reasonable time.

Hence it becomes necessary for the solution of some uric-acid stones, and for all oxalate of lime stones, to discover some way of exposing the gravel or calculi to the action of stronger agents than dilute lithia or soda.

In the 'Philosophical Transactions' for 1852, p. 201, I have shown what can be done out of the body by disengaging nitric acid and potassa in contact with uric acid by the help of the voltaic battery. Although this is easy in glass vessels, it is very difficult to make a catheter that can cause this action to take place within the bladder; and after months spent in producing an instrument fulfilling all the electrical conditions for success, the equally essential surgical conditions are by no means perfect. There is a want of firmness and fixedness of the blades which make the introduction of the litholitic instrument difficult. Still, when surgeons skilled in electrical science, and possessed of sufficient time and patience, arrive, I have little doubt but that uric-acid calculi will be dissolved in the bladder. Some more energetic substances may be

liberated in contact with the stone, or some way may be found of rendering the stone more soluble. At present progress is stopped more by the mechanical than by the chemical difficulties of the problem.

Oxalate-of-lime gravel or calculi are so hard and so insoluble that as yet there is no prospect of obtaining any good results by any process of solution. But oxalate is so closely related to carbonate of lime, and this last is so rapidly soluble in any dilute acid, that hopes must be held firm that some day a process of oxidation may be carried on in the bladder to compensate for the want of that oxidizing action in the blood and kidneys which leads to the formation of this kind of stone.

LECTURE VII.

DISEASES OF SUBOXIDATION.—ON GOUT.

The gouty diathesis consists in an excess of urate of soda not only in the serum of the blood, but in the fluid that diffuses from it into all the vascular and non-vascular textures of the body. An attack of gout is a chemical process of oxidation set up in the parts where the urates are most able or liable to accumulate. By the oxidizing action the urates are wholly or partly changed into urea and carbonates, which can more readily pass from the textures into the blood, and be excreted by the kidneys, skin, and lungs. The oxidation even in the bloodless textures causes increased flow of blood and mechanical pressure in the vessels nearest to the inflamed part, and hence pain and redness, and then swelling and œdema, proceed. Though the gouty diathesis is a disease of the textures as well as of the blood, yet in its origin and situation an attack of gout is even more a disease of the tissues than a disease of the blood.

The urate of soda bears the same relation to gout that sugar does to diabetes; and as the want of oxidation of sugar is the cause of the diabetic diathesis, so the want of oxidation of the urates, and their consequent accumulation in the textures and blood, is the cause of the gouty diathesis. Errors excepted, as almost every grain of starch passes through the stage of sugar, so almost every grain of albuminous substance that enters the blood sooner or later, in its way out, passes through the stage of uric acid, and, if thoroughly oxidized, escapes as urea, carbonic acid, and water. The number of substances that are formed between albumen and urea are vastly more than between starch and carbonic acid; but, whatever their number, there must be an antepenultimate, and uric acid is the penultimate, and urea the ultimate, product of oxidation. Hence there are at least two ways in

which an excess of uric acid may occur in the blood and textures; 1st, from an excess of animal or vegetable albuminous food entering the system,—*i.e.*, from excessive production; and 2nd, from an arrest of oxidation,—*i.e.*, from want of destruction. Of course, the greatest accumulation of uric acid will occur when the albuminous food is excessive, and when at the same time the oxidation is least. Even if no excess of albuminous food is taken, yet if the oxidizing action is deficient, uric acid may accumulate in the serum, and it will immediately diffuse even into the bloodless textures. On the other hand, an excess of albuminous food may be taken, and, provided the oxidizing action is also in excess, no accumulation of uric acid in the blood or textures may occur. It is therefore evident that there are two modes of preventing the gouty diathesis: 1st, by diminishing the amount of vegetable and animal albuminous food; and 2nd, by promoting oxidation. In other words, the smallest amount of food and the greatest amount of air are the antidotes for the gouty diathesis. If an excess of fresh air is taken whilst a large quantity of food is eaten, these cause no gouty diathesis as long as the antidote (oxygen) destroys the *materies morbi* (urates, or the substance out of which urates are formed); but if from any cause the oxidation becomes less, the future or formed urates accumulate in the liquor sanguinis, and pass by diffusion into and around the cells of all the vascular and non-vascular structures of the body, and remain unoxidized where there is least oxidation, and even form crystals of urate of soda in consequence of the slow deposition of the urates on the surface and within the structure of the non-vascular cartilages. Where urate of soda accumulates it acts like a foreign body, increasing friction, setting up irritation and inflammation, by which the uric acid is more or less oxidized, and thus being made soluble, it is more or less removed, and when the inflammation subsides, effused fibrin almost alone may remain to mark the situation of the attack.

If no inflammation comes on, the liquor sanguinis may free itself of urates by the kidneys, and then the deposited crystals may more or less entirely re-dissolve, and diffuse back into

the blood; or, if the serum continues full of urates, the chalk stones may gradually increase in the direction of least resistance, making the joints more and more rigid, and the skin more and more thin, until the pressure breaks the surface, and the chalk stones escape as myriads of microscopic crystals. Thus, the fingers and toes may become supplementary kidneys, to the great relief of the blood and textures, and the gouty diathesis may almost be considered as microscopic gravel in the textures, and an attack of gout as a chemical operation for the removal of the gravel from the part in which it had accumulated.

That the urates diffuse into the synovial fluid and on to the surface of the cartilages, the following case shows:—W. W., aged 48, was admitted into St. George's Hospital on November 23, 1855. He was a painter and glazier in good circumstances, and had suffered more or less from gout for eighteen years; otherwise he enjoyed good health, and never had colic. The urine contained a small quantity of albumen; the heart's action was feeble; the right hand was red and swollen; his feet were slightly œdematous; chalk stones existed in his ears. The acute attack of gout in a fortnight gradually subsided, and he was about to leave the house when a fresh inflammation of the hands, feet, and knees came on, with great prostration of strength. In a few days he was seized with epileptic fits; the slightest motion immediately brought on an attack; the pupils were contracted, there was excessive tremor of the limbs, and he sank four weeks after his admission.

Both knee-joints were carefully opened. They contained two or three drachms of thick synovia, and in each cavity there was a flake of fibrin about an inch and a-half long, shreddy, with whitish specks visible to the naked eye. On examination under the microscope, small acicular crystals were seen mixed with fibrinous matter, and when a drop of dilute hydrochloric or acetic acid was added, the whole surface of the fibrin in a few minutes became covered with microscopic uric-acid crystals. The moist fibrin from both joints showed these crystals of uric acid, and when the fibrin was treated

with nitric acid and evaporated, there was distinct evidence of uric acid. On the surface of the cartilage there was only a very small spot free from the deposit of urate of soda. Both great toes at their tarso-metatarsal articulations contained the same deposit on the surface.

The spleen was large and soft; the kidneys granular, and the cortex much wasted. There were some small deposits of red sand visible to the naked eye in the mammary processes.

A man, aged 41, was admitted into St. George's Hospital with continued fever, and died on August 20, 1849. On examination by Dr. Handfield Jones, gouty deposit was found in both knee-joints: 1st, under the synovial membrane at the margin of the cartilage; 2nd, in the superficial structure, or on the surface of the cartilage, from whence it could not be removed by gentle washing or scraping; 3rd, in the substance of the cartilage at some depth; 4th, in the cancelli of the subjacent bone (the patella).

The gouty matter appeared for the most part as aggregations of amorphous masses, varying in size, and encrusted over frequently with minute crystalline spiculæ.

The cartilage was remarkably thickened, being at least three times its ordinary dimensions. Near its middle it was much more elevated than towards its margin, and very soft and yielding. When a vertical section was made of it, the surface exhibited a marked fibrous structure, quite visible to the naked eye, the fibres being arranged vertically to the surface, and being much more marked in the deeper than in the superficial layers.

The microscope showed that the basis substance was considerably increased, the cells being in much scantier proportion than natural, but not essentially altered. The fibres were not isolated from each other. The fibres or bands were of some considerable width, separated by narrow intervals of healthy structure.—*Proceedings of Pathological Society*, vol. ii., p. 103.

On the Means of Detecting Gout.

The chemical test for the gouty diathesis—that is, for excess of urates in the blood and textures—is based on analysis of the urine and of the serum of the blood.

Even long before the gouty diathesis is formed, the urine will give warning of the future disease. From the latest experiments an excess of urea in the urine is caused only by an excess of vegetable or animal albuminous food. The amount of urea bears no certain and no direct proportion to the amount of daily exercise; so that an excess of urea in the urine chiefly indicates that albuminous food in excess is passing through the system; when the oxidation of the albumen is perfect, urea and carbonic acid are formed; but with less perfect oxidation, urea and oxalic acid result. Hence, oxalate of lime, with excess of urea, constitute the earliest evidence of imperfect oxidation of an excess of albuminous food. When the oxidation is still less, then oxalic acid and urea are not formed from the uric acid, but the urine shows an increase in the quantity of urates.

Simple inspection of the urine is quite worthless as a means of determining the amount of urates in the urine, for the clearest urine may have the greatest amount of urates dissolved in it, and urine that thickens on cooling may contain less uric acid than perfectly clear water. You will see in a paper I published in the 'Philosophical Transactions,' Part ii., 1849, p. 249, that urine passed at 5.10 p.m. became thick on standing, and contained 0·52 grain uric acid per 1,000 grs. urine; urine passed at 11 p.m. remained clear on standing, and contained 0·87 grain uric acid per 1,000 grs. urine. Again (p. 251), urine passed at 7.35 p.m. became thickish on standing, and contained 0·29 grain uric acid per 1,000 grs. urine; urine passed at 10.5 p.m. remained clear on standing, and contained 0·33 grain uric acid per 1,000 grs. urine. Again, urine passed at 7.55 p.m. became thickish on standing from urates, and contained 0·31 grain uric acid per 1,000 grs. urine; urine passed at 10.45 p.m. remained clear on

standing, and contained 0·90 grain uric acid per 1,000 grs. urine.

When analysis shows that an excess of uric acid is thrown out of the body, this is a proof that the gouty diathesis is ready to form whenever the kidneys cease to remove the excess from the system. The presence of any urates at all in the urine is a sign that oxidation is not so perfect as it might be, and the more urates in the urine the more imperfect the oxidation in the system must be considered; but as long as the products of the imperfect oxidation are thrown out by the kidneys or skin no gouty diathesis is produced.

Thus, then, first, excess of urea in the urine; secondly, oxalate of lime with excess of urea; and thirdly, urates in excess, by analysis, constitute the three tests of the different degrees of suboxidation which precede the establishment of the gouty diathesis.

When uric acid in excess is in the system, analysis of the urine may not indicate any excess there—indeed, the uric acid may be absent from the urine and be retained in the blood—as, for example, in Bright's disease. Then the chemical examination of the serum may give positive proof of the existence of this imperfect oxidation, and lead to the certainty of the textures containing the same urates ready to set up inflammation of a gouty nature at any moment; usually symptoms of gout begin to make themselves felt by pain, followed by heat and redness, and then the chemical methods for detecting gout are usually quite unnecessary.

On the Symptoms of Gout.

The blood when loaded with urates varies every moment in the quantity of these crystals which it contains, and in its power of keeping them in solution; moreover, every moment by diffusion some of the urates pass with the nutriment and oxygen into the textures. The oxidation in the blood and textures may balance the supply or fresh formation, and no accumulations or congestions may occur until some medical or surgical accident—that is, some sprain or injury, some cold

or other accident, as, for example, even an apoplectic attack—happens to determine the flow of blood or nutriment to any one part more than the rest; then and there gouty deposit and inflammation will be set up.

When no accident is the immediate cause, some ordinary occurrence may be sufficient to give rise to the gouty inflammation—thus a long walk, a tight shoe, a full meal, a strong dose of medicine, a fright, will determine the commencement of the local action, which may be of any degree of mildness or intensity. Thus it may be limited to a continuous feeling of burning and tenderness in the feet, or even to a few passing twinges in the great toe or heel, that may last only a few minutes; or it may fall upon one joint after another and produce an amount of suffering and general fever with a degree of redness and heat, and ultimately of swelling of the surface, that may surpass the products of any ordinary inflammation.

When the effusion which constitutes most of the swelling takes place from the vessels the tension in the capillaries is relieved, and the violent action becomes less.

Usually, the gout, like an abscess, fixes on one spot, and there remains until the whole attack is over; but as in pyæmia abscesses may occur in any number outside the blood-vessels as in the joints, so also when urates in excess are in the blood and textures they may set up congestion and combustion in any part, either successively or simultaneously, according to the amount of urates that diffuses into any part.

The pain arises from increased sensibility of the nerves, produced by the increased flow of blood from the oxidizing action which is going on in and around the painful nerve; and this increased action is fed by the increased flow of blood in every part where complete obstruction does not occur; so that the pain is the best measure of the local symptoms. The general symptoms will vary with the age, sex, constitution, temperature, idiosyncrasies, and unsoundness of the patient. The same amount of urate poison in the blood and textures may in different persons produce totally different effects, and

these will vary in the same person according as the combustion is slow or rapid; in other words, according as the attack is chronic or acute.

There is nothing in the general or local symptoms that can enable the eye to tell that any inflammation is certainly gouty; any other inflammation in the same parts will at first have precisely the same local and general symptoms, though the history of the attack will generally, though not always, lead to the truth. Thus secondary inflammations from traumatic or idiopathic pyæmia may be easily mistaken for gout.

Rheumatic inflammation so closely resembles gouty inflammation in all its local and general phenomena that no positive differentiation between the two diseases can be made, except in the *materies morborum.* The rheumatic poison has not yet been isolated; that it differs from uric acid in its solubility, and probably in its volatility, is shown by its not forming calculi, not depositing itself visibly on the joints, escaping by the skin and giving rise to local symptoms when the secretion of the skin is checked by cold and wet. In the analysis of sweat, as yet only one acid that at all approaches to uric acid in composition is known—sudoric or hidrotic acid ($\text{Є}_5H_8N\text{Θ}_6H_2\text{Θ}$?). It may be that this is the rheumatic poison, and that an excess of it in the blood causes the rheumatic diathesis, and its local oxidation a rheumatic attack. But whatever the acid, there is no reason why the rheumatic and gouty acids should not coexist in the same blood, causing a rheumatic-gouty diathesis; nor why a local oxidation of both acids should not take place at the same time in the same part, constituting an attack of rheumatic gout. Certainly there is no positive proof as yet that this happens, but animal chemistry is still very young, and will speak much plainer on this and many other subjects when grown up. Meanwhile, the rheumatic poison exists as surely as the scarlet fever poison, and a skilful chemist may at any moment isolate both.

The local symptoms and the general symptoms of gout, rheumatism, and rheumatic gout closely resemble those of an ordinary inflammation, but there is a very important difference

in that these specific inflammations are set up and modified in their course by the presence of specific substances in the textures that take part in the peroxidation. Hence, as soon as these substances are destroyed by oxidation in any part, or generally, the symptoms disappear from that part or from the body, and are transferred to another place or entirely subside. Thus the rate of transference is a measure of the intensity of the local action and of the amount of poison in the textures. In the severest attacks a few hours finds the seat of the inflammation changed, whilst in a very slight attack one joint may be slightly affected for months continuously.

There is another great difference between ordinary inflammation and rheumatic or gouty inflammations. In these specific inflammations pus comparatively rarely forms, while an excess of fibrin in rheumatism, perhaps even more than in gout, exudes wherever local action is taking place. How far this deposition of fibrin is connected with the peculiar oxidation of rheumatic and gouty inflammation, animal chemistry has to determine; certain it is that only in the weakest and most debilitated constitutions, in those in whom the actions of nutrition and oxidation are most imperfectly carried on, does pus in any quantity form either in the gouty or in the rheumatic inflammation.

The history and the causes of the attack usually furnish the means of determining the nature of the inflammation, but ultimately animal chemistry will tell with perfect certainty whether gout, rheumatism, rheumatic gout, or some other modified combustion is going on in the blood and textures. Even now Dr. Garrod has shown how from a few drops of serum obtained from a blister, uric acid, by its insolubility in dilute acid, may be proved to be present or absent; and who can foresee what new methods of quantitative or qualitative analysis of urates or sudorates may be discovered?

Professor Stokes by spectrum-analysis can trace the oxidation or deoxidation of the blood-globules, and we are beginning to recognize differences in the chemical composition of the sun and the fixed stars, and to determine the chemical and physical constitution of the nebulæ; whilst, by the same

means, even the twelve-millionth of a grain of lithium can be detected in distilled water, and the six-millionth part of a grain in the urine or in the textures.

On the Complications and Consequences of Gout.

As the gouty diathesis arises from urate of soda in the serum and serous fluid which passes out of the blood into every cell, so in every vascular as well as non-vascular texture urates may accumulate and set up an exaggerated process of oxidation so as to cause more or less severe inflammation. In the vascular textures the accumulation of urates is very unlikely to occur, and when it does happen, rapid circulation quickly causes an oxidation which removes the urates and restores the part to a healthy state.

An excess of urates while passing through the capillaries of the kidney is liable, like silver or other metallic poison, to be caught in the texture of the kidney, and to set up parenchymatous nephritis, which causes permanent organic disease.

Many of the complications of gout arise from some functional or structural disease to which the patient is liable independently of the imperfect combustion of the urates in the tissues and blood. If any function or structure be wrong, the disturbance produced in the system by the local oxidation of the urates will, in some cases, increase the previous wrong action, and thus complicate the attack of gout.

Still, in other cases the counter-irritation, derivation, and purification of the blood and textures from urates by oxidation do remedy previous disorders; but there is a reverse truth which frequently makes itself evident in the increased suffering and weakness produced by an attack of gout accompanying or following some other disease. So that an attack of gout instead of being always a cure, is sometimes an aggravation of other ailments.

A gentleman about 70 years of age was entirely deprived by an apoplectic attack of the use of his right side. Two days after the stroke the most violent gout came on in his right

foot. The violent pain in the foot caused constant involuntary motion of the limb, over which he had no control. The paralytic state of the limb had no influence over the progress of the attack of gout, but the involuntary motion increased the suffering from the gout fearfully, but did not hinder his ultimate recovery.

A gentleman, 73 years of age, was under treatment for irritable bladder, dependent on chronic inflammation of the prostate; he had been confined to the house for some days by frequency and pain in voiding water, when violent gout came first in one foot, and when this subsided quite as severe an attack came in the other foot, disabling him for three weeks. Throughout the attack the irritability was even worse than before the gouty attack, and after the gout ceased there was no immediate improvement in the state of the bladder.

A gouty gentleman had for some months complained of pain in his head when he coughed, or sneezed, or shook his head, and without any cause he had become deaf. This lasted for two months, and was attributed to latent gout. He caught a very severe cold, which confined him to his bedroom, and the third or fourth evening he suddenly became comatose. He could not be roused to take his medicine or his food, and he passed his water under him. Active counter-irritation was used to the neck and extremities, and in the morning violent gout came in one foot, and he lost his head symptoms entirely. The gout was most intense in every joint of the body, and it was more than a month before he could move. When he began to drive out, he again began to complain of his headache when the road was rough; this increased, and in three or four days he again became very heavy, and before a week was over he died perfectly comatose, the attempt to bring out the gout again entirely failing.

The great mechanical consequence of gout is the loss of voluntary motion from the joints becoming fixed. The progress is from the toes and fingers through every joint to the jaws. I have seen a patient unable to stand for sixteen years —unable to move either hand or arm except to the slight

degree that enabled him to sign his name somehow; unable to open his mouth except for very small morsels of food; unable to turn his head in any direction—a recumbent statue, with moving eyes, and heart, and diaphragm, sloughing from the constant pressure which he was unable to remove, while never-ending pain wore down the system until it was unable to resist a complication of diseases.

On the Treatment of Gout.

In the present state of our knowledge the treatment of gout may be divided into two parts: first, the specific; and second, the expectant treatment. Each method has its own advantages and disadvantages, and by the right use of both proceedings the greatest good with the least harm may be attained.

The specific treatment aims to get rid of the attack as soon as possible; that is, to put an end to the pain at once; to stop the fibrinous and crystalline thickening of the joints, and to allow the patient to return to his usual mode of life in the shortest possible time.

The disadvantages of this treatment are, first, that the specific sometimes acts more violently than is intended; and secondly, that cutting short an attack leads more quickly to a return of the disease, because the usual mode of life is that which has caused, and therefore will again cause, the gout; and thirdly, that the urate of soda existing in excess in the serum and diffusing into all the textures, where it is oxidized, if stopped in its active oxidation in any part, is more liable to set up a process of active oxidation in the fibrous textures of some internal organ, as the stomach, the brain, or the heart.

The expectant treatment aims to keep the gout fixed in the extremities until the textures and blood are freed as much as possible from the urates by oxidation, and to effect a long-continued change for the better in the usual mode of life, at least during the illness; and from both these causes a long interval is likely to intervene between the fits of gout.

The disadvantages of this treatment are, first, that the

patient may get very feeble from the long-continued inflammation and confinement, and that out of this other ailments may thus arise; secondly, that the joints, in consequence of the duration of the inflammation, may become much more thickened by fibrin and urates than they otherwise might be, and that thus also the general health may give way from the loss of exercise.

The value of the specific treatment is seen when some more important organ than a joint is attacked by violent gouty or rheumatic inflammation. Then, to avoid irreparable injury to the organ, the specific inflammation must be stopped as quickly as possible. Acute inflammation of the eye furnishes by far the most striking example of the use of colchicum. By the specific treatment the eye may be saved; by the expectant treatment it will be lost; and the activity of the specific treatment must bear a direct proportion to the intensity of the inflammation. In a slight attack the expectant treatment alone may be required, but in a violent outburst the most energetic specific treatment, even with the help of local or general bleeding, will scarcely be able to preserve the sight of the inflamed eye.

The specific treatment consists in giving colchicum, veratria, sabadilla, and different quack medicines the composition of which is unknown, but which probably contain one or other of these remedies.

By far the most popular specific is colchicum; and if the action of this substance was fully known the action of all the other gout specifics would be understood.

There is no question that the alkaloid colchicine is the active substance in colchicum; and though this substance is not yet isolated and analyzed, there are good grounds for belief that it closely resembles veratrine, perhaps as closely as quinine does cinchonine.

Colchicine	=	$\mathrm{C}_x\,\mathrm{H}_y\,\mathrm{N}_2\Theta_z$.
Veratrine	=	$\mathrm{C}_{32}\mathrm{H}_{52}\mathrm{N}_2\Theta_8$.
Strychnine	=	$\mathrm{C}_{21}\mathrm{H}_{22}\mathrm{N}_2\Theta_2$.
Quinine	=	$\mathrm{C}_{20}\mathrm{H}_{24}\mathrm{N}_2\Theta_2$.
Cinchonine	=	$\mathrm{C}_{20}\mathrm{H}_{24}\mathrm{N}_2\Theta$.
Morphine	=	$\mathrm{C}_{17}\mathrm{H}_{19}\mathrm{N}\,\Theta_3$.

It is very evident that the analyses of these different alkaloids give no clue whatever to their medical properties; and so the analysis of colchicine will give no explanation of the mode of its action. But, however much these alkaloids differ in their action, they all have this in common, that they act energetically on the nervous system.

The problem to be solved is, how does colchicum stop the excessive oxidation set up in the parts where the urates are most liable to accumulate, partly, perhaps, in consequence of the non-vascular nature of the textures?

That colchicine acts as a diuretic, and throws the uric acid out of the blood, is not capable of proof, and if it were it would not give any explanation of its action on the joint. That colchicine promotes the oxidation of the uric acid by directly furnishing oxygen, as peroxide of lead might do, is contrary to all chemical probability. There remains the unproved assumption that colchicine, like these other alkaloids, acts on Dr. Liebreich's protagon, that the alkaloid has a chemical action by actual contact with the nerve substance of the blood-vessels, where the gouty inflammation is going on, causing such an action on the vessels that the inflammation ceases.

This assumption makes the action of colchicine comparable with the action of veratrine, strychnine, and morphine, all of which act with intensity on the nervous substance; and this assumption leads to a conjecture as to the action of quinine, that it also may act on the nerves of the blood-vessels, stopping the internal congestion, on which the external rigor of ague depends. The deafening and prostrating effects of large doses of quinine can arise only from an action on the auditory and cardiac nerves, and the arrest or prevention of an ague fit can best be comprehended by the assumption that quinine, among other actions, acts on the nerves of the capillaries, stopping congestion; whilst colchinine acts on the same system of nerves, stopping inflammation.

M. Roudanowski has stated to the Académie des Sciences that, after poisoning animals by strychnine, nicotine, opium, and chloroform, he has detected by the microscope changes in

the nerve-cells or in the myeline; but his observations cannot yet be received as conclusive.

In M. Laville's specific, veratrine is probably the active alkaloid; most probably a small amount of morphine is also dissolved in the wine with which it is prepared. It is said to be made from sabadilla seed, but whatever the source or nature of the alkaloid, it must have an action corresponding to colchicine, and the good and the harm from this specific cannot be much more nor less than the good and the harm of colchicum. It cuts short the attack, and thus saves the injury to the joints from the continuance or severity of the inflammation; but it does this by stopping the oxidation of the urates in the textures, and hence a relapse or renewal of the inflammation more quickly and easily takes place.

Moreover, like all other specifics, it gradually loses its effect when it has been used in many attacks; and one at the least of those who have been its most public supporters have abandoned it for some fresh, though far less potent, remedy.

Used in half-drachm doses every four hours, or one drachm doses twice or thrice daily, it acts often most decidedly. If anything, it causes less action on the stomach, and more action on the bowels than colchicum, and from the disposition to drowsiness which it frequently occasions, probably the irritative action is moderated by some opiate.

There can be little question that colchicine used by subcutaneous injection into the neighbourhood of the inflamed part would put an end to the attack; but the danger of an overdose would, perhaps, be greater than when taken in by the stomach, and the benefit derived from its use would not compensate for the fear of its abuse. It would probably act more quickly and more strongly than when taken into the stomach, but this rapid relief would be gained at much greater risk to life from the alkaloid acting on the nerves of the heart and causing dangerous syncope. Moreover, relief from pain and time for the full action of the colchicine when taken by the mouth may be obtained by the subcutaneous injection of one-fourth or one-third of a grain of acetate of morphine in

ten or twelve minims of water into the neighbourhood of the inflamed joint.

Late one evening I was sent for to a gentleman suffering with a most violent attack of gout in the knee; the heat and the pain were excessive. There was some swelling and some redness. The attack had begun in the previous night, and had increased in intensity all day. I injected the third of a grain of morphine into the inside of the thigh near the knee, and gave a drachm of Laville, ordering another drachm to be taken when he awoke. He slept for upwards of six hours without waking, and he seemed very certain that but for the injection the night would have been passed in even more agony than the day. After four drachms of Laville the attack subsided, and the following night no morphine was required.

In sciatica the use of the subcutaneous injection is most beneficial; sometimes almost whilst giving the morphia the pain subsides, and in eight or ten minutes drowsiness comes on, and sound and continuous sleep follows; but the alkaloid acts more strongly than when taken into the stomach, and an overdose may easily be given, and the poison is beyond the reach of an antidote.

The expectant treatment consists in preventing the accumulation of the urates in the serum and textures, and in promoting its elimination and oxidation.

The accumulation of urates is greatly to be prevented by a strict diet, chiefly as regards the quantity of animal and vegetable albuminous food that is eaten.

The elimination of urates is best effected by washing the serum and textures—that is, by increasing the flow of urine by means of water and diuretics. When the serum is comparatively free from urates, then the urates in the textures diffuse back into the blood and may be thrown out.

The oxidation of the uric acid in the textures and blood can be effected directly or indirectly by air, diet, and medicine.

So that the expectant treatment consists of diet, to prevent accumulation of urates, and to promote their oxidation; diuretics to promote their elimination; and air and medicine to promote their oxidation.

During and after an attack of gout, when thickening of the joints exists, medicines that promote the absorption of the effused fibrin and serum are very useful. Of these iodine externally and iodide of potassium with alkalies internally are the most efficacious. Iodine, perhaps, acts indirectly as an oxidizer.

But first of the diet in twenty-four hours :—

Let us suppose that the minimum diet of health may be represented by 10·5 grammes (162 grains) of soluble nitrogen, and 240 grammes (3696 grains = 8 ounces nearly) of soluble carbon—

If 1 ounce of meat when cooked contains 77 grains of nitrogen and 92 grains of carbon ; or,

If 1 egg contains 16 grains of nitrogen and 118 grains of carbon,

And 1 ounce of butter contains 355 grains of carbon,

And 5 ounces of dry bread contain 38 grains of nitrogen and 592 grains of carbon,

And 21 ounces of arrowroot contain 3633 grains of carbon,

Then it is easy to see that 2 ounces of dry meat, and 2 eggs, and 14 ounces of bread will give more nitrogen than the system requires to repair ordinary losses, and the excess may have to be thrown out, partly in the form of urates, when the oxidation is insufficient to produce urea.

If 2 ounces of dry meat or 2 eggs only are taken, about 10 ounces of butter would be necessary to furnish the fuel and power for the system, or an equivalent quantity of fat must be absorbed from the stores deposited in the cellular tissue. Or, if 5 ounces of dry bread only were eaten, then above 9 ounces of fat must be taken up in twenty-four hours ; but a diet of 2 ounces of dry meat, and 2 eggs, and 5 ounces of bread, requiring the wasting of the body by 7 or 8 ounces of fat daily, could not long be endured. Moreover, these quantities of nitrogenous food produce more urates than a less nitrogenous diet would do.

If a little more than 21 ounces of dry arrowroot were taken daily, this would supply more carbon than is lost in the daily oxidation. The excess of carbon must either be deposited as

fat, or must take away the oxygen, so as to leave none free to act on the nitrogenous substance that is passing out from the albuminous textures. Hence, with carbonaceous diet in excess, the whole of the uric acid from the tissues might pass off through the blood unoxidized.

It follows, then, that in gout a minimum of albuminous food should be taken in order to produce the least uric acid; and a minimum of carbonaceous food in order to allow the uric acid to be oxidized as much as possible.

If a pint of ordinary beef-tea, free from fat, contains 46 grains of nitrogen and 160 grains of carbon, and if an ounce of dry arrowroot contains 175 grains of carbon, then $3\frac{1}{2}$ pints of beef-tea and 18 ounces of arrowroot will contain the full amount of elements that are required even in health for the system, and far less than this would be desirable when the minimum production of urates is required.

Secondly as to air :—

In oxygen the energy exists without which all our heat and all our power, and, indirectly, if not directly, all our growth would stop. The nitrogen of the air probably only dilutes the oxygen to the strength we can bear. Some experiments of M. Regnault's show that in less dilute oxygen more of this gas is not inhaled than in our atmosphere. M. Pettenkoffer will probably give us more accurate knowledge of this subject, and enable us to see the amount of intermediate oxidations going on within the body by comparing under natural conditions the total amount of oxygen that goes in with the amount that comes out in the carbonic acid and water that are the products of the ultimate oxidation only.

The use or uselessness, in the treatment of gout, of the inhalation of oxygen and of ozone can be determined only by the most careful experiments. At present, voluntarily increased rapidity of respiration in fresh air (blowing the fire, in other words) is likely to add more oxygen to the blood than strengthening the mixture of oxygen artificially.

The oppressive and debilitating effect produced by the respiration of air heated to the temperature of the blood proves that diluting the oxygen by expansion produces a very decided

effect on the oxidizing action in the body. The hotter the air, the less will be the amount of oxygen in a given space; and the colder the air, the more oxygen will the lungs obtain. Moreover, the diffusion of the gases in the vesicles and the bronchial tubes must be greatly influenced by the different temperatures of the different parts of the column of air. The purer the air the less carbonic acid, and the less mineral, vegetable, and animal impurities will it contain in the form of dust. Any increase in the amount of carbonic acid in the inspired air produces a chemical impediment to the escape of carbonic acid from the blood, and the passage of smoke and dust into the air-vesicles themselves mechanically interferes with the actions of solution and diffusion on which respiration depends.

When reaction can be set up, then cold air (or cold water) promotes oxidation; but continued external cold directly or indirectly causes contraction of the vessels of the surface, and drives the blood within; and hence the greatest oxidation takes place by keeping the circulation free on the skin and extremities by the warmest possible clothing, by enveloping the inflamed part in cotton and oil-silk, or in flannel.

Thirdly, on the action of medicines in promoting oxidation, elimination, and absorption.

For indirectly promoting oxidation the two most potent medicines we possess are alkalies and iron. Alkalies assist in the oxidation of organic substances, not by giving oxygen, but by promoting the formation of vegetable and animal acids, and ultimately forming carbonates out of the burning matter. Familiar instances are the saponification of fats, the use of caustic potash in Trommer's test for sugar, the use of lime in Moore's test; the use of potass in Liebig's method of determining the amount of oxygen gas by pyrogallic acid.

Hence caustic alkalies, potass, soda, magnesia, are more efficacious as oxidizers than carbonates, and carbonates more potent than bicarbonates. But even bicarbonates, when heated with organic substances, lead to the formation of organic acids, which displace the carbonic acid, and thus

promote the oxidizing action. Thus diabetic sugar with sulphate of copper and carbonate or bicarbonate of potash in the cold gives no reduction, but when heated to 212° the reduction is evident. Ammonia is at least partly oxidized in passing through the system, and therefore it is of no avail in the treatment of gout as an oxidizer, though it may be used to neutralize acid in the stomach, or to act as a temporary stimulant.

Iron indirectly is an oxidizer, by its power of drawing oxygen into the blood. The great object of giving iron as medicine is the formation of blood-globules. For this hæmoglobin itself would probably be the best preparation, as being nearest in composition to the substance ultimately formed; but hitherto all attempts to prepare even hæmatin in quantity as a medicine have failed, and dried colouring matter of the blood is the simplest substitute. The reduced metal, the oxide, the carbonate, or some vegetable salts, are usually given, and all with good effect. The large amount of iron that passes off in the fæces and urine shows how little metal attains the intended object. In ten minutes I have found a solution of sulphate of iron passing out in the urine, and in twenty-four hours in the fæces. Hence very small doses of hæmoglobin would probably be equivalent to the large doses of other iron medicines which are given. In the active state of gout iron of any kind is inadmissible; in the passive state it becomes a most efficacious remedy.

All the salts of the organic acids that pass through the stomach into the blood, as, for example, the acetates, tartrates, citrates, are oxidized and pass into the urine and textures as carbonates; and hence all effervescing saline draughts may be considered as acting in the tissues as the carbonates of the alkalies act; that is, they promote the formation of organic acids in the textures; and these acids pass by the absorbents, and by the veins back into the blood, to be oxidized and thrown out by the urine and by the skin.

The mineral waters, reputed good for gout, are mostly dilute solutions of alkali—*e. g.*, Vichy water. Generally the stronger the water the more efficaciously it acts, but the

action of the water itself must not be disregarded—*e.g.*, Buxton; the water diffuses not only into the urine, making that more dilute, but it dilutes the serum of the blood, and diffuses into the textures, dissolving deposited urates, and hindering fresh deposition of crystals. Thus water alone in sufficient quantity acts not only as a diuretic, but as a dialytic remedy, and in gout the action of the water of mineral waters might be still more exactly defined as urilytic. The water takes the uric acid as urates from the textures and carries it to the blood to be oxidized, and thrown out as urea and carbonic acid.

In the gouty deposits, however, there is another substance—namely, fibrin, which is by no means soluble like the urates, for water and alkaline carbonates have but little action on deposited fibrin. How far iodine, bromine, and mercury possess the power of indirectly or directly oxidizing fibrin has yet to be determined. In the present state of our knowledge, nitrate of potass is of all remedies the one which can pass readily into the joints, and which may exert a solvent action on the fibrin that may be deposited there.

On the Secondary Mechanical Diseases that arise from the Wrong Chemistry of Gout.

The accumulation of urates from the want of oxidation in the textures, and the deposition of fibrin in and around the joints, gradually produce more or less complete loss of motion. In extreme cases, after each attack of gout a lower degree of locomotion is reached by the patient. The stiff fingers and toes are followed by stiff ankles and wrists, and these by stiff elbows and knees, which generally fix the patient in the sitting position. Then the hips and shoulders become affected, and the jaws will scarcely open to allow solid food to pass. Ultimately, even the neck loses much of its mobility.

These different stages may be reached gradually and successively; or many stages may be passed through in a single attack. When once a joint has become fixed, very little liberty of motion is afterwards regained, but by persevering

endeavours to extend and to flex the joint, in spite of the pain which the attempted motion causes, more use of the limb may be got than at first sight might be thought possible. As soon, however, as a fresh attack of gout comes on, far more motion usually is lost than had been regained.

The consequences that result from the more or less complete loss of motion may be divided into two classes. The first are mechanical, and the second chemical, and these are so connected the one with the other, that it might perhaps better be said that the effects are mechanico-chemical and chemico-mechanical.

The mechanico-chemical effects may be seen in almost every texture of the body.

In the skin the inability to relieve the pressure of one part on the other or of any part on the surrounding matter causes fresh irritation, and then ulceration; so that sores will form wherever the pressure is greatest.

In the cellular tissue the uniform position causes the veins to become distended, increased effusion into the cellular tissue occurs, and the absorption of fluid is diminished, and œdema in the legs and sometimes in the arms may be observed.

In the glandular organs the loss of exercise causes diminished flow of blood through the textures, and hence diminished secretion of bile, urine, saliva, occurs.

The chemico-mechanical effects of complete loss of motion are seen in increased loss of oxidation and nutrition in all the vascular and non-vascular structures of the body.

In the skin, dry or moist eczema very frequently occurs.

In the muscles, the muscular fibre so wastes and fatty matter so takes the place of contractile texture, that even if the joints were free to move, the muscles themselves are so changed in chemical composition that they become ultimately unfit for work.

Then the tendons contract, and the shortened muscles drag the limbs and extremities into outrageous distortions.

In the blood-vessels and cornea, atheroma and the arcus senilis, even in comparative youth, give evidence of the low degree of nutrition and oxidation that is taking place in the textures.

In the glandular blood-vessels—as, for example, in those of the kidney—the same alteration occurs. Some of the components of the urine remain in the blood, while the albumen of the blood passes into the urine. Thus one of the consequences of the gout tends to reproduce the cause of the gout.

The very bones undergo changes of nutrition from the ossicles of the ear to the thigh-bones, at first thickening in parts, with increased vascularity, whilst elsewhere increased earthy deposit gives an ivory hardness; afterwards absorption may occur in places, so that the trochlea of the humerus or the neck of the thigh-bone may be more or less completely absorbed, and the form of the bones may thus be entirely changed.

At first the nerves and the brain seem the only parts of the body unaltered, but increased sensibility aggravates the sufferings of the patient. Then comes great irritability, with want of decision; then loss of perception or false perceptions amounting to hallucinations, of which the patient himself may be perfectly conscious. If the strength of nutrition returns, all these symptoms may entirely disappear, showing that no permanent alteration of the nervous centres has occurred.

Thus the original chemical disease of suboxidation of the urates may cause such an entire loss of mechanical power that not even a crumb of food can be raised to the mouth or a fly can be driven away from the skin, and death would soon result from the debility of starvation, if external force was not made to compensate for that which cannot be produced within.

But gradually the textures deteriorate and the fluids stagnate, and debility or dropsy mechanically put a stop to the sufferings which the wrong chemistry had originally produced.

LECTURE VIII.

DISEASES OF SUBOXIDATION.—ON THE XANTHIN AND CYSTIN DIATHESES.

In the previous lectures I have dwelt on a few of the different diseases arising from different degrees of sub-oxidation of sugar and albumen. If you call to mind how out of the body very many different substances may be produced by different degrees and kinds of sub- and peroxidation of organic substances, you will see that in the body it is probable that innumerable different substances may also be produced, depending on slight variations in the circumstances under which these oxidations take place.

In the oxidation of coal, for example, different series of substances are produced by different variations of the circumstances under which the oxidation proceeds. Professor Hofmann, in his Report on the Exhibition of 1862, mentions fifty-one different substances produced by destructive distillation of coal alone, and many more products have been obtained since that time.

There can be no doubt but that in different parts of the body different series of substances are formed by different degrees of oxidation of the albuminous substances of the body. For example, the very small amount of oxygen that reaches the liver influences the formation of a series of totally different substances from those that are produced in the kidneys rich with oxygen. The sulphocyanogen that is formed in the salivary glands indicates a different oxidation from that which occurs in the lachrymal glands. The substances produced by oxidation in the spleen from the different mechanical structure of the organ will be different from those produced in the supra-renal capsules. The oxidation that takes place in the muscles depends on the amount of oxygen

and the composition of the muscle, and so the muscles will give rise to substances that will differ from those produced in the nerves, and so of each portion of the body.

If our knowledge permitted, we might draw up different series of substances produced in each part of the body, and each series might begin with the least oxidized and end with the most oxidized that could be produced under the different circumstances in which the oxidations proceed; and each series would vary according to the substance oxidized, the supply of oxygen, and the more or less perfect and continued contact of these with one another.

Our knowledge is so little advanced that the place or places where the different substances are produced are very inexactly determined. That some of the uric acid is produced out of the kidney, and that this in the kidney is oxidized into urea and oxalic acid, or urea and carbonic acid, cannot be doubted. It is also most probable that some substances, as, for example, leucin or creatin, or both, are the antecedents of the uric acid produced in the textures, and in the kidney. Whatever the substances may be from which the uric acid is formed, and wherever the oxidation may occur, chemistry can prove that in some rare occasions a slight arrest of oxidation takes place partly or wholly, and instead of uric acid xanthin is formed; and this substance has been detected because it forms one kind of calculus—in other words, because it is capable of producing a mechanical disease.

The following table shows the relationship of xanthin to uric acid, and also shows the less oxidized product immediately preceding the formation of xanthin:—

Sarcin or hypoxanthin, $\text{Ɵ}_5H_4N_4\text{Θ}$, occurs in the liver, spleen, and probably in the kidneys.

Xanthin, $\text{Ɵ}_5H_4N_4\text{Θ}_2$, occurs in the liver, spleen, and sometimes in the urine.

Uric acid, $\text{Ɵ}_5H_4N_4\text{Θ}_3$, occurs in the muscles, glands, and always in the urine.

In all the proportion of nitrogen to carbon is the same—that is, four to five; whilst the proportion of nitrogen to carbon in urea is as two nitrogen to one carbon, showing

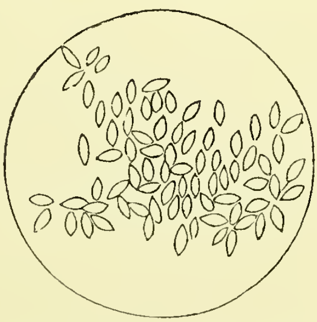
that in the formation of urea the removal of carbon, probably as carbonic acid, must have occurred. The pathological condition that obtains wherever and whenever xanthin is produced is similar to that which leads to the diseases I have previously brought before you—namely, suboxidation.

Xanthin arises from imperfect or insufficient oxidation of the products of albuminous matter. As in diabetes, so here, the cause of this imperfect oxidation is still unknown; but the direction in which the cause must be looked for, and the means of prevention, if the chemical error were a frequent one, is very clear. It is probable that in young persons varying conditions are much more likely to occur than in the middle-aged, and hence youth is the time in which the greatest chemical variations in the working of the body are most likely to be found. Thus it is in youth that xanthin, and probably also cystin, will most frequently be formed. In middle or old age the same variations of oxidation may sometimes occur, for cystin has been found in the urine of old people, although hitherto xanthin has only been met with in the young.

On the Means of Recognizing the Xanthin Diathesis.

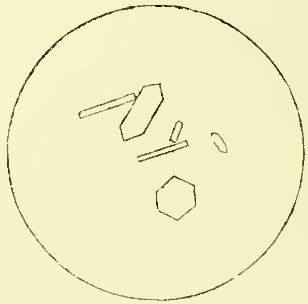
The following case was published in the 'Journal of the Chemical Society' in 1862:—"In July, 1861, I was consulted regarding a schoolboy, nine years and a-half of age. The following history was given to me. He had good health until three years old, when he was seized one night with violent sickness and pain in the stomach, which continued incessantly for three days. Neither mustard-poultices, blisters, nor leeches relieved the pain nor stopped the sickness. The third day his water gradually became the colour of blood; it then stopped altogether, and nothing was passed for four days; then delirium and convulsions came on, and these lasted for twenty-four hours, when he was relieved by a most violent perspiration. No stone was seen to pass. In a few days he was perfectly well, and continued so for nearly three years, when in June, 1861, he caught a slight cold, and was delirious

one night. A medical man saw him, and found some albumen in the urine, which then was generally thick, and the quantity of deposit was increased by excitement or temper. Cold produced the same effect in a less degree. He never complained of pain in the back, and was able to take more exercise than other boys of his age without fatigue. He always had a good appetite, and was allowed to eat everything. On examination, I found a very small quantity of albumen in the water made at night, and none in that made in the morning. There were no blood-cells, no tubular casts, and the specific gravity was high. I examined many specimens without finding anything remarkable. About the end of July, when he was leaving London, a small vial of urine was sent to me, which was quite thick and deep-coloured. A drop was placed under the microscope, and a crystalline deposit was found resembling one form of uric acid. From the form I considered the



deposit was uric acid. On examining the unfiltered urine for albumen by heat, I was surprised to see the crystalline deposit entirely dissolve. A fresh portion of sediment showed the same crystalline appearance and the same solubility by heat. This was so utterly unlike any uric-acid deposit, that a closer examination of the sediment was made, but so little substance was left that no satisfactory conclusion could be arrived at, except that it was not uric acid. A day or two afterwards another specimen was brought to me containing the same crystalline deposit soluble by heat. The sediment formed about an eighth of the bulk of the fluid. It was collected on

a filter, washed with alcohol, and it gave the following reactions:—It dissolved in water and in hydrochloric acid; when treated with nitric acid, it dissolved without effervescence, and when evaporated to dryness, it left a yellow residue. When the solution in hydrochloric acid was evaporated to dryness it left beautiful minute crystals of this form:—



These crystals were soluble in water. The sediment was easily dissolved by alkalies. The watery solution of the sediment had a feebly acid reaction, and, when evaporated to dryness, left an amorphous residue, which was again easily dissolved in water. These reactions agree only with the latest and best observations of the reactions of xanthin. Hoping to get more of the substance, I wrote to the country for the sediment of the urine. It was collected on many occasions, but I could only find urates and uric acid, and none of the crystalline deposit soluble by heat. In January, 1862, the same boy was brought to me, with two specimens of urine and four different dried deposits; and at different times for three weeks I examined the urine. It was generally of high specific gravity—1026, 1026, 1027, 1030; once as low as 1013. It sometimes contained a trace of albumen. Usually it contained urates, and sometimes uric acid and oxalate of lime, but never the crystalline deposit soluble by heat. The dried deposits consisted of urates and uric acid, and one of them consisted of phosphate of lime, with a little phosphate of ammonia, and magnesia, without a trace of uric acid or xanthin."

In the summer of 1863 I could find no albumen in this boy's urine, and his health was very good. In the summer of 1864 he appeared quite well when he was brought to me. No xanthin could be found on either occasion.

The stone which Langenbeck removed at Göttingen was from a boy also. The most minute portion of this stone which I have examined did not allow me to determine the form of the crystals so as to identify them with those I found in my patient.

Although in this case albumen was present in the urine, yet I consider that it probably bore no relationship to the first crystalline deposit which was found. As in the production of uric acid in albuminous urine, there are two different causes in action, producing two different effects, which may have no connection whatever, so I consider in this case the albuminous urine depended on some altered condition of the kidney, possibly on a previous renal attack, whilst the xanthic-acid crystals depended on a very rare degree of suboxidation. The slightest degree more of oxidation would have given uric acid. The least degree less would have given hypoxanthin. In the varying changes of oxidation in the body it is most unlikely that that degree should be long kept which produces xanthin; and on this, its rarity and probably its short continuance as a diathesis depend.

Other gravel occurring at the same time and afterwards, and probably causing renal calculus two years previously, point also to a deficiency in the oxidizing actions in the body. The following year, in this boy, urates, uric acid, and oxalate of lime were found appearing separately or simultaneously for three weeks, during which I had very frequent opportunities of examining the urine. If these substances are considered to be products of different degrees of suboxidation, when the oxidation was least, the uric acid formed; when the oxidation was somewhat more, uric acid and oxalate of lime appeared; when there was still more oxidation, oxalate of lime alone was produced; whilst in some very rare degree of oxidation between the degree that caused uric acid and that which causes oxalic acid, the peculiar substance xanthin was

formed, and lasted only until a different degree of oxidation was set up.

The treatment, then, of xanthin is identical with the treatment of uric acid or of oxalic acid. It consists in promoting oxidation—first, by diet; secondly, by exercise and clothing; and thirdly, by medicine. I need only recapitulate here the need of little fuel in the food; much oxygen from cool, fresh air; warm clothing to promote circulation; and, lastly, alkalies and iron. These will probably quickly stop the formation of xanthin, if it ever comes before you. Very possibly from the appearance of the crystals it has often come and gone, and been throughout regarded as uric acid.

On the Cystin Diathesis.

The production of cystin in the body must depend on a very much lower as well as a very different process of oxidation of albumen from that which produces uric acid and its derivatives. The composition of cystin is $C_3H_6NO_2S_2$. The proportion of nitrogen to carbon is four to twelve, whilst in uric acid it is four to five, and in urea it is four to two. Twelve, five, and two may be taken as the indices of the different amounts of suboxidation in cystin, uric acid, and urea.

Even in the secretions of the body in health traces exist of the want of oxidation of complex sulphur bodies. Thus, in the bile and in the saliva sulphur compounds exist. Taurin from the liver has the composition $C_2H_7NO_3S$, and sulphocyanic acid from the salivary glands contains CNHS. It is in the highest degree probable that these substances are not built up in the body, but are the products of the disintegration of the albumen.

In consequence of peculiar and as yet unknown conditions, the sulphur of the albumen is only partly oxidized, and one portion is left combined with the other elements, giving rise to cystin, or taurin, or sulphocyanic acid.

Hitherto I have tried in vain to discover the relationship of cystin to uric acid and urea by means of the products of its decomposition.

I was given by Dr. Percy a considerable piece of cystin, but it proved insufficient to admit of a determination of that relationship which chemistry will one day make clear. Some of the results of my experiments may be mentioned here.

Cystin when boiled with hydrochloric acid is not decomposed. Treated with oxide of silver, it is decomposed very slowly. Sulphide of silver, sulphate of ammonia, and an uncrystallizable yellow substance, very soluble in water, is obtained.

When nitrous acid is passed through water which contains cystin it is rapidly dissolved with effervescence. The acid solution contains sulphuric acid; when this is neutralized with carbonate of baryta and filtered, the filtrate gives, with nitrate of silver, chloride of mercury, and acetate of lead, a white amorphous precipitate insoluble in water. When the silver precipitate is well washed with water, and decomposed by sulphuretted hydrogen, and filtered, a solution is obtained which leaves a residue of an oily consistence, and acid reaction when evaporated in a water-bath. When this is boiled with carbonate of zinc, filtered, and evaporated, a gum-like residue is obtained, very soluble in water, with a feebly acid reaction.

Among these products of the decomposition of cystin none of the ordinary substances occurring in the urine except sulphuric acid were found. Perhaps this was from the want of sufficient material to operate upon, but more likely because cystin may arise from and pass down through a totally different series of oxidations from uric acid.

Since the paper by Dr. Ronalds on unoxidized sulphur and phosphorus in the urine (see 'Phil. Trans.,' 1846, p. 461), it has been thought that possibly some substance related to cystin, if not cystin itself, might be found to be present always in the urine. In regard to this sulphur substance, also, I have only obtained negative results, having failed to isolate this unoxidized sulphur body in the urine. It certainly is not cystin; it escapes precipitation by acetate of lead and basic acetate of lead and ammonia; even in this last precipitate,

from one litre of urine only very little unoxidized sulphur could be found.

If the clear fluid from the ammonia precipitate has the lead separated by hydrochloric acid, and is then evaporated and burnt with nitre, chloride of barium gives a considerable precipitate. If, instead of being burnt, the fluid is evaporated, and then mixed with so much oxalic acid that all the lead and all the urea are separated, and if the excess of oxalic acid is removed by lime water, and the liquid then filtered and evaporated and extracted with ether, sulphuric acid is obtained. If after this a syrupy solution of chloride of zinc is added and left to stand a short time, then a crystalline precipitate of creatin in chloride of zinc is formed, but no sulphur body is thus obtained.

Another method was followed in the endeavour to isolate the unoxidized sulphur body. The urine was precipitated by the lead salts and ammonia, the urea was separated by oxalic acid, and the hippuric acid by ether. On evaporation a brown-coloured fluid like a syrup was obtained. Lime water was added until the reaction was alkaline. The fluid was then filtered from the oxalate of lime and evaporated as far as possible. After standing four days crystals appeared, and after standing some days longer all the fluid became solid. These crystals, however, contained no sulphur; very probably they were crystals of inosit, and thus again the sulphur body for the present escaped from me.

The amount present is indeed very small, for seven ounces nearly of urine contained only 0·5 grain of unoxidized sulphur (200 c. c. of urine contained sulphur 0·5 grain. 150 c. c. contained sulphur 0·38 grain).

When cystin is present in the urine the unoxidized sulphur body of healthy urine is certainly not increased; this may be proved in many cases, even when the cystin diathesis has continued for years. From such cases it is clear that the cystin diathesis does not imply a very deteriorated state of health, for the patients may follow their ordinary occupations and hardly ever ask or require medical advice.

On the Complications of the Cystin Diathesis with Other Disorders.

All the usual deposits in the urine may occur when cystin is present there, and the examination of calculi shows that phosphates, oxalates, and urates may co-exist with cystin. In other words, the cystin diathesis does not render the simultaneous formation of other products of suboxidation impossible.

When the bladder becomes diseased, mixed phosphates may be deposited with the cystin, as in a large cystin calculus in St. Bartholomew's; and the larger the stone, the more likely the bladder is to become affected. In the large stone—two and a-half inches long by one and three-quarter inch broad—in the museum of University College, phosphate of lime only co-exists, showing that the urine was nearly neutral, but that the bladder was not diseased.* Oxalates with the cystin may be found on examination of the urine by the microscope, although I do not recollect any mixed calculus of cystin and oxalate of lime.

A young man, about 25, had been troubled with gravel when ten years old, for which he was attended by Dr. Prout for three years; he remained tolerably well, though delicate, until three months before I saw him, when, with great suffering, he passed a cystic-oxide calculus. He was also troubled with nocturnal emissions, and the urine on examination contained cystin with crystals of oxalate of lime; it was feebly acid, pale, and of low specific gravity.

How different the accompanying deposits and state of the urine may be is well seen in the following case :—In a middle-aged lady the urine was highly acid, and thick from deposition of red urates; specific gravity, 1027·9. When filtered, it was of a bright yellow colour, with a rather peculiar, but not very marked, smell; examined by the microscope, it contained multitudes of small and large cystin crystals, single and in masses, with amorphous urates in very considerable quantity. To the filtered urine, acetic acid was added, and a

* See 'Medico-Chirurgical Transactions,' 1840, p. 193.

very plentiful amorphous precipitate fell; on standing, this deposit gave uric-acid crystals. The addition of nitric acid to the unconcentrated urine produced crystals of nitrate of urea.

The co-existence of cystin diathesis and granular disease of the kidney is well shown in the following case:—

An Italian courier, aged 45, consulted me November 22, 1848, for hæmorrhage from the kidney for three weeks, which, he said, had been stopped by drachm doses of tincture of steel. He said that he had constantly, for twenty years, passed calculi, many at the same time, and that they resembled sugar candy; that he had had frequent attacks of hæmaturia; that he had some pain in the loins, and the small quantity of urine which I could obtain contained many pus globules and much albumen, and was feebly acid to test-paper. Specific gravity, 1023. There was no œdema of the legs. No effusion in the chest; and no signs of disease of the heart. Fourteen months afterwards I again saw him. He was drowsy, and rapidly became comatose, and died January 26, 1850.

The body was well formed, and in good condition. The kidneys only were examined.

On cutting open the left kidney, one large calculus and some smaller pieces were found there; all consisted of cystin. The calculus was not loose in the pelvis, but adhered, requiring to be cut out before it could be removed. The mammary processes of the kidney were absorbed, and the chief part of the cortical structure was much encroached on by the stone. The irregular cavity formed by this dilatation of the pelvis contained some highly offensive purulent fluid. The left ureter appeared to be pervious, though it was thickened, and the lining membrane was inflamed.

The right kidney was very small, being less than one-half its natural size. It was remarkably diminished in thickness. The capsule was firmly adherent, and when removed the cortical substance was very rough with a granular beaded appearance. No urinary cysts were observed in it. On section, the cortical structure was very much wasted, and of a very deep colour. A considerable quantity of fat was sur-

rounding both kidneys, closely adhering to the capsules of the kidneys and to the surrounding tissue. The mucous lining of the bladder near to its neck was somewhat more vascular than natural. No other morbid appearance was observed.

When the cystin diathesis tends to the formation of stone, the mechanical disease in no respect differs from that produced by any other concretion. Though the cystin stone is one of the softest and most elastic of all stones, so much so that a large stone for some days at least after its removal from the bladder is distinctly compressible and elastic between the finger and thumb, yet the mechanical symptoms cystin causes do not appreciably differ from those which the hardest of all stones, oxalate of lime, occasions.

The deposition of cystin calculus can only occur when the urine is neither highly acid nor highly alkaline; and though no instance has as yet been recorded of the solution of a cystin calculus whilst in the bladder, yet if the urine is feebly alkaline, dilute warm hydrochloric acid caused to pass through the bladder by means of a double catheter would rapidly dissolve the stone; or if the urine was over-acid a warm dilute solution of carbonate of potass would have very great solvent power on this kind of stone. As phosphates are apt to be precipitated when the stone is large, at first dilute acid should be used; and after some time, when the stone decreases, dilute alkalies should be employed to dissolve the stone by passing in quantity through the bladder.

On the Treatment of the Cystin Diathesis.

The conversion of cystin into sulphuric acid, carbonic acid, and urea, though not at present accomplished out of the body, is perhaps one of the constant chemical transformations occurring within. The treatment of this diathesis, like that of all the other diatheses which I have brought before you in this course of lectures, consists in increasing the oxidizing action in the body. The indication to be followed is the same as in the treatment of diabetes, oxalic acid, uric acid, and xanthin; but

as cystin implies a much greater degree of deficiency of oxidation, so the oxidizing treatment must be much more energetically carried out in this than in the other errors arising from suboxidation of the albuminous substances. Perhaps, for comparison, I might say that cystin stands in nearly the same position to the albuminous food that sugar does to the amylaceous food, and that the smallest degree of oxidation of these two classes of food may give rise to two homologous diseases apparently so different as the cystin and saccharine diatheses.

In concluding this first part of my course, let me say that the mutual relationship which I have endeavoured to point out between diabetes, acidity, uric acid, gout, oxalic acid, xanthin, and cystin, and the influence of one and the same cause in their production is so startling, and our knowledge of animal chemistry is as yet so incomplete, that I cannot hope to bring conviction quickly to the minds of all; but I am sure that many and great additions will be made to the evidence of suboxidation which I have given you on each of the subjects on which I have dwelt; and if I had taken diseases of the liver and other organs, I might have multiplied greatly the number of diseases that ultimately will be proved to arise in the body from suboxidation.

Whether you adopt my theoretical views or not, you will find a practical gain by endeavouring by food, by air, and by medicine to produce an increase of oxidation in the treatment of these different complaints. In a short time probably much more will be known regarding the action of ozone in the body; and be not of the number of those who think no more of oxidation in health and disease than they are compelled to do by the grand fact that oxygen goes in with the air, and that carbonic acid comes out in the breath as long as the patient lives, and whatever the state of health or of disease may be.

Hitherto the healthy and the morbid structure of the body has formed the chief object of medical scientific investigation, and the forces which do all the work in these structures have hardly yet got their first fundamental basis fixed in the fact

Stearic	$C_{18}H_{36}O_2$		
Balenic	$C_{19}H_{38}O_2$		
Arachidic	$C_{20}H_{40}O_2$		
Nardic	$C_{21}H_{42}O_2$, or	1 Nardic	$C_{21}H_{42}O_2$
Cerotic	$C_{22}H_{44}O_2$		
Melissic	$C_{23}H_{46}O_2$		

Diatomic Fatty Acids.

Carbonic	$C\ H_2\ O_3$, or	6 Carb. acid	$C_6H_{12}O_{18}$
Glycolic	$C_2H_4\ O_3$, or	3 Glycolic	$C_6H_{12}O_9$
Lactic	$C_3H_6\ O_3$, or	2 Lactic	$C_6H_{12}O_6$
Butilactic	$C_4H_8\ O_3$, or	$1\frac{1}{2}$ Butilactic	$C_6H_{12}O_{4\frac{1}{2}}$
Phocic	$C_5H_{10}O_3$		
Lucic	$C_6H_{12}O_3$, or	Lucic	$C_6H_{12}O_3$

Fat may be considered as a combination of fatty acid and glycerine; by superheated steam, by alkalies, by strong acid, by peculiar ferments formed in the pancreas, liver, and bowels, the neutral fats are decomposed, and the fatty acids are set free from the glycerine. All the fatty acids and the glycerine, when oxidized, ultimately give rise to carbonic acid and water.

Cholestearin, $C_{52}H_{44}O_2$, in some respects resembles glycerine. It occurs in the bile, blood, brain, spleen, and in all kinds of cysts and chronic abscesses; and it is also met with in vegetables. It is a fatty substance, but its full relationship to other fats has not yet been determined.

Every part of the body, each particle of every part, contains more or less of some kind of fatty matter. No animal substance exists which will not give fatty matter when treated with ether. Chemical analysis is unable at present to determine accurately all the differences in the mixtures of fatty matter from different parts; but differences are detectable by the eye, and the terms waxy, fatty, lardaceous, oily, are used to denote variable mixtures of olein, stearine, &c. To the chemist these eye examinations are full of uncertainty and untrustworthy; for the greatest errors have been and will be made by guessing at quantitative and qualitative analyses by looking at substances with or without the microscope. The waxy-looking matter no more makes real wax than milky chalk and water makes milk.

I may here for a moment mention a corresponding error in

regard to amyloid or starch-like matter. The so-called starchy substance is in no respect related to starch; instead of being a hydrocarbon, it is a nitrogenous substance, and a modification of fibrin, and has nothing whatever to do with amyloid substance, and has no claim to a name which entirely misrepresents the composition of the effused substance.

There are at least three different conditions, under any of which fatty deposit is likely to occur in any part of the body. First, fat is likely to be deposited when an excess of fat food, or of food capable of becoming converted into fat, is taken into the body. In such circumstances the amount of oxygen which passes into the body is insufficient to oxidize the excess of fatty matter, and consequently it accumulates and is deposited in the cellular tissue. The fattening of man and animals, from aldermen to Strasburg geese, demonstrates the general state of suboxidation from this cause on which the accumulation of fat depends.

Secondly, fat is deposited when no excess of fatty food is taken, but when the conditions of oxidation locally and generally are so reduced that the ordinary amount of substances taken as food and capable of becoming fat are not oxidized.

Thirdly, fat accumulates and may be deposited when, from imperfect oxidation, the nitrogenous substances—albumen, fibrin, gelatine—do not pass down, through alkaloids, acids, and neutral substances, into urea and sugar, or urea, carbonic acid, and water, but give rise to fatty products of decomposition in consequence of an imperfect supply of oxygen. The least oxygenated substances, as sugar and fat, are thus produced; and the most carbonaceous fatty substances are formed by the least supply of oxygen.

These three conditions, which, separately or together, determine the deposits of fatty matter, mark three different degrees of suboxidation in the body. In the first degree there is no deficiency of oxygen, but oxidizable materials are in excess, whilst in the second and third degree there is a deficiency of oxygen which is insufficient to make, first, the non-nitrogenous, and, secondly, the nitrogenous oxidizable substances pass off in the most perfect state of combustion.

First, when there is an excess of non-nitrogenous food with no deficiency in the supply of oxygen, the deposit of fat which arises becomes excessive, and constitutes a general disorder; and as some remarks on this general state will make the local deposition of fat more intelligible, I shall occupy your attention with it before passing to the consideration of the local disease.

In my first lecture I have already pointed out the relationship of the fatty to the saccharine diathesis. The evil that results from excess of farinaceous and saccharine food, and the good that immediately follows from omitting these substances from the food marks the strong resemblance between these very different complaints. The difference between them is well shown in the good which cream, butter, oil, and fat effect in diabetes, and in the harm which results from these articles of diet when there is an excess of obesity.

Innumerable experiments have in the last few years been made on the reduction of the fat of the body by abstinence from starch, sugar, fat, and butter; and on the increase of weight scarcely less conclusive experiments have been made by giving cod-liver oil to human beings, and oil-cake or fattening food to animals.

For example, Mr. Banting, by leaving off "bread, butter, milk, sugar, beer, and potatoes," reduced his weight from 202 lbs. to 156 lbs. in fifty-two weeks.

Mr. Lawes states that by fattening, oxen increase in fat from 16 to 30 per cent.; sheep, 18 to 23; pigs, 22 to 44. "Starch and cane sugar have nearly equal fattening values, and fat or oil have probably about two and a half times the value of starch for the purpose of storing up of fat in the body."

The second cause is too little oxygen to burn the non-nitrogenous food. This becomes apparent in the ordinary fattening of advancing years, when with no change of diet the amount of air and exercise falls so far below the proportion it should bear to the food eaten that a deposition of fat takes place. I have already pointed out how, in old age, under the same circumstances, sugar in small, but distinct excess is apt to occur in the urine.

The want of oxidation and the deposit of fat consequent on destruction of the blood-globules is another instance of the action of this cause. To this I shall shortly return.

The third cause is want of proper oxidation in the nitrogenous substances. This has been assumed as the special cause of fatty degeneration. Observations upon the production of so-called adipocere and microscopic examinations of textures have led to the belief that fibrin forms adipocere, and that syntonin instead of splitting into inosit and kreatin, gives rise to fatty and nitrogenous matter. The following results obtained by Dr. Ormerod are worthy of attention, though in the progress of chemistry the word "margarine" will not be used, and "adipocere" will entirely disappear.

"The amount of fat present in healthy beasts, chiefly margarine, varied from 0·22 to 2·14 per cent. In decidedly fatty animals the oily matter varied from 0·48 to 2·74.

"A weighed portion of healthy muscular substance of the heart exposed to a slow stream of water gave no adipocere.

"A weighed portion, containing 2·14 per cent. of fatty matter, chiefly margarine, left to soak for twenty months in dilute nitric acid, specific gravity 1·42, gave only 1·1 per cent. fat.

"Two hundred and fifty grains of fibrine from bullocks' blood, freed from all fat by ether, treated the same way and for the same time, gave no trace of fat.

"A portion of muscular substance, containing 2 per cent. of fat, was left for eight months in dilute alcohol (1 to 7). At the end of this time it contained 1·92 per cent. of fat."

In every local deposit or production of fat, one or all of the three causes of general fatty accumulation are in action. Locally, either there is an excessive supply of fatty matter, or the ordinary amount of non-nitrogenous food is not consumed in the textures because the oxidation is deficient; and when this occurs the sugar even may part with some of its oxygen, and pass into some higher carbonaceous fatty compound; or, thirdly, from insufficient oxygen, the nitrogenous substances of the body—albumen, fibrin, syntonin, gelatin—instead of passing through urea and sugar into urea and carbonic acid

and water, may give rise to one or many less oxidized series of products of decomposition by which more or less highly carbonaceous fats may be produced.

Local deposits of fat without general deposit probably rarely occur from excessive supply; but when this cause acts together with imperfect oxidation, then local deposits and productions of fat take place anywhere. The vast local deposits of fat which constitute fatty tumours depend chiefly on the existence of a cyst in which the process of oxidation is at its lowest point. Whatever fatty matter is brought to the cell remains unchanged, and if an excess of fatty matter is taken, the deposit of fat increases in proportion to the quantity of fat that is brought within the cyst. When the imperfect oxidation extends to the nitrogenous substances, then in a few hours even the texture of a part may be entirely changed by the insufficient supply of oxygen.

The chief cause of insufficient oxidation is insufficient supply of oxygen from insufficient supply of red blood, and this depends on insufficient pressure of the circulation, insufficient iron, and a thickened condition of the internal capillaries belonging to the part; in other words, on mechanical and chemical imperfect actions. Probably the most striking instance of acute fatty disease that I can give you was published by Rokitanski in 'Zeitschrift der Wiener Aerzte,' No. 32, 1859:—

A girl tried to poison herself by phosphorus matches. She was soon sick, and, after this, appeared well. In a day or two she appeared slightly jaundiced; soon after she became wandering, had dark brown vomiting, and convulsions; on the sixth day she died. On post-mortem examination, the body was well nourished; the skin yellow; the membranes and brain bloodless. In the throat, bloody, frothy, very tough mucus. In the pleuræ, mediastina, and base of the heart, ecchymoses, in some places of considerable extent; a slight pleuritic effusion on the left side. Lungs full of blood. Liver to a high degree fatty, pale yellow-reddish, pasty, and empty of blood. In the gall-bladder and gall-ducts, a slimy fluid. The mucous membrane of the stomach swollen, and containing

a brown, thick fluid. In the small intestines, a brown, bloody, pappy stuff, and in the large, some matter more lumpy. The spleen small and brittle. The kidneys large, very light yellowish-white, slightly jaundiced, apparently very fatty. In the bladder there were a few drops of a thickish yellowish fluid.

Microscopic examination of the kidneys showed that the epithelium of the tubes of the cortical structure was distended with small and large fat cells, and the tubes themselves were full of fat.

Another case of a girl of 13, who poisoned herself with phosphorus, has been reported by E. Wagner, who found not only a remarkable increase of fatty matter in the liver and kidneys, but also in the muscular structure of the heart and in the muscular coat of the small intestines and bronchial tubes.

The discovery of a relationship between fatty liver and poisoning by phosphorus has led to a multitude of experiments on animals during the last four years in Germany and in France. Of all these, the work of Dr. Munk and Dr. Leyden on 'Acute Phosphorus Poisoning' contains the most striking experiments, and leads to the most distinct proof of the influence of the state of the blood-globules in the deposition or production of fatty matter.

Frogs had phosphorus dissolved in oil injected under the skin; they died in two days, and the liver and kidneys and flesh of the heart were fatty. Rabbits had the phosphorus of from five to twelve phosphorus matches, or 1 to 2½ c.c. (6 grs. to 1 oz.) of oleum phosphoratum injected into the stomach; they died mostly in two or three days, but even in one day the liver and kidneys were always fatty, and the muscular structure of the heart was frequently so. Dogs killed with small doses of phosphorus showed the same deposit of fat in the liver, kidneys, and muscular structure of the heart. In rabbits ecchymoses were found in the pleuræ and in the texture of the lung and bloody urine, in one case without a trace of blood-globules. In dogs ecchymoses in the heart and blood-stains in the mediastinum and gums and blood throughout the bowels. Whether these symptoms are

produced by the phosphorus as such or arise from some of its compounds had then to be determined.

After poisoning by phosphorus in no part of the body could the most delicate test detect phosphorus, nor could the authors find any action of phosphorus on the blood-globules out of the body, so they made a strong solution of 8 or 9 grains of phosphorus to the ounce, and injected this (2 or 3 c.c.) into the blood of rabbits and dogs. Phosphorus acid vapours in each case were expired through the nostrils, violent inflammation was set up in the lungs, but none of the peculiar signs of phosphorus poisoning were produced. Further experiments were made to prove whether phosphoretted hydrogen and hypophosphorus acid were the poisonous substances, but neither these substances nor phosphorus acid produced the effect. With this last acid, specific gravity 1·12, they made experiments on frogs and rabbits, and though it proved poisonous, yet it did not dissolve the blood-globules; and .after poisoning by phosphorus, phosphorus acid could not be detected in the organs by the most careful research. There remained then the action of phosphoric acid. Experiments were made with frogs, rabbits, and dogs. Phosphoric acid, specific gravity 1·16, was used, and 1 or 2 to 6 c.c. of this acid were injected under the skin or into the stomach or jugular vein, and the effects on the blood, on the heart and circulation, on the respiration, on the stomach and bowels, the kidneys, liver, and the nerves and muscles were determined.

The blood-globules were dissolved as by the bile acids; extravasations of blood were frequently found. The pressure of the blood in the jugular, measured by the manometer, was seen to sink after the injection of the acid. The temperature of the blood fell. The muscular structure of the heart became granular and even distinctly fatty, whilst the transverse striæ disappeared.

When the acid was injected into the stomach the strongest marks of corrosion of the mucous membrane extended to the small intestine. The kidneys were congested, and the epithelium of the tubes was distinctly fatty; the urine became albuminous, with blood and fibrinous cylinders. The liver

became most evidently fatty. In short, the phosphoric acid, with the exception of the local symptoms of erosion and jaundice, produced all the symptoms and appearances which phosphorus itself does when it acts as a poison.

Having thus shown that after poisoning by phosphorus no phosphorus, phosphoretted hydrogen, hypophosphorus, or phosphorus acid can be found by the most delicate tests, and that phosphoric acid will give rise to all the symptoms and appearances which phosphorus produces, it remained only to show how phosphoric acid acted.

The action of phosphoric acid is twofold—first and chiefly, on the blood-globules; and secondly, on the nerves and muscles.

Any substance that can dissolve the blood-globules produces the greatest derangement of their functions, and this affects the nutrition and oxidation going on in the different organs. We may even assume that the great mass of the blood-globules by the action of acids would lose their power of nutrition and their property of taking up oxygen before they would become perfectly dissolved. The heart more especially shows the effect of the altered (unoxygenated) blood in its power of work; and the voluntary muscles are not less sensible of its influence. Great feebleness, tremor, and paralysis result. The functions of the nerves are interrupted, and coma and convulsions finally appear. These phenomena may chiefly be set down to the want of nutrition and oxidation in the different organs, in consequence of the altered state of the blood. Although a part of the effect may result from the direct chemical action of the phosphoric acid on the different substances that exist in the nerves and muscles.

In other directions, the effect of altered (unoxygenated) blood on nutrition and oxidation can be made evident. The authors, in a paper on poisoning by sulphuric, nitric, oxalic, and tartaric acids, have shown that all substances which dissolve or destroy the blood-globules cause fatty metamorphosis of the tissues and organs. The direct mixture of the poison with the blood is the most important determining cause, the fatty appearances being most evident in the experiments on

that force, like matter, is indestructible; whilst the inquiry how far the forces of the body proceed from the chemical actions which take place within (instead of being considered as opening a new and a great field for investigation) is denounced almost as a heresy, for which extreme perpetual peroxidation would be too poor a punishment.

To some of my hearers who hold that in all idiopathic fevers "the nervous system (and particularly the sympathetic and vagus) is paralyzed," and that in inflammations the dilatation of the blood-vessels by one-third or more of their diameters depends on a paralysis of the vasomotor nerves, the omission from these lectures of the term nervous force will prove a fatal objection; but my object has been to treat these diseases as chemical questions, in order that it may appear how much and how far chemistry can add to our knowledge of these complaints; but there is in the distance a question which greatly concerns these diseases, and which involves the action of the nervous force, and this, in conclusion, I must shortly bring before you.

On what does the want of oxidation of which I have been speaking depend?

I may state the answer to this question thus:—Suboxidation occurs if the fuel is excessive, if the oxygen is deficient, and lastly if the conditions for the action of the chemical forces in the oxygen and fuel are unfavourable. It is regarding this last determining cause that the question of the action of the nervous force arises.

In the salivary glands the experiments of Ludwig, Bernard, Eckhard, and Schiff show that two kinds of vasomotory nerves exist:—1st, those that close the artery—these proceed from the sympathetic; and 2nd, those that enlarge it—these come partly from the facial and partly from the trigeminal nerve.

When by irritating directly or reflexly the closing nerve little blood passes through the salivary glands, then the production of saliva is at its lowest amount; whilst by irritating directly or reflexly the trigeminus, the blood flows freely through the capillaries, even so as to admit the pulse to be

seen in the veins; the venous blood becomes red, and the secretion of saliva becomes most free.

The capillaries generally throughout the body are subject to the vasomotory action of the sympathetic nerve. When the sympathetic is irritated, the capillaries contract to the uttermost, and the circulation is retarded; and when the sympathetic is paralyzed, the capillaries become dilated to the greatest degree possible, and the circulation is accelerated.

Thus this vasomotory action of the nerves affects the passage of the blood in the blood-vessels, and oxidation is promoted or retarded as the circulation becomes quicker or slower.

It may be said that the nervous force, without the intervention of any action on the blood-vessels, can exalt or depress the conditions necessary for oxidation and increase or diminish the oxidizing action in the capillaries and in the cells which are nourished by the liquor sanguinis. Without hesitation the vitalist adopts this view. The chemist, on the contrary, will admit it only when animal chemistry is so far advanced that it can be proved that the quantity in which the active substances are supplied, and the rate of removal of the products of the action are clearly insufficient to account for the increased or diminished oxidation which in these different circumstances is found to occur.

PART II.

ON LOCAL CHEMICAL DISORDERS ARISING FROM SUBOXIDATION, AND THEIR MECHANICAL RESULTS.

LECTURE IX.

EFFECTS OF INTENSE COLD—FROST-BITES—CHILBLAINS—GENERAL AND LOCAL FATTY DEPOSIT AND PRODUCTION.

In all the general chemical disorders arising from suboxidation which I have brought before you, some one or more parts of the body might have been found in which the imperfect action more particularly occurred. Thus, for example, acidity might be shown to be sometimes greatest in the stomach, sometimes in the skin, and sometimes in the kidney. Or urate of soda might be observed to accumulate sometimes in the hands, sometimes in the feet, sometimes in the ear, according to slight determining causes which escape our notice. Indeed, no strict line of separation between general and local disorders of chemical action in the body can be drawn; for when general disorder exists, local manifestations of that disorder are sure to arise, and when a local wrong action is taking place, this, by contact with blood-vessels and nerves, insensibly passes into a general disturbance, and this contagion can be traced in all the chemical actions of health as well as in the errors which excess or deficiency of chemical action occasion.

Thus, in the chemical disorders arising from local suboxidation, a general want of action may usually be traced out which either modifies or aggravates the local affection, and when this general want of action becomes still more marked, symptoms are produced quite as important as those that occur in the diseases that formed the subjects of the first part of this course of lectures.

For clearness, I have hitherto endeavoured in the lectures on general diseases of suboxidation to make a separation between the chemical disorders connected with the oxidation of the body and the chemical disorders connected with the repair of the body; but in local diseases it is soon seen that no separation between these actions is possible. Mortification from cold cannot be separated from senile gangrene, nor fatty deposit from disuse or insufficient supply of blood from fatty deposit from diseased vessels. Oxidation and repair take place in the same part at the same time, and errors of oxidation and errors of nutrition are so dependent each one on the other that in local or limited disorders the actions cannot be separated. And the perfect picture of any disease will only be obtained when our knowledge of the chemistry of nutrition and the chemistry of oxidation in the affected part are both equally perfect.

I might well have chosen the general action of cold as furnishing the best possible introduction to this course of lectures, inasmuch as it offers the most striking demonstration of the dependence of life on chemical action; but I shall dwell on the general action of cold now only so far as will enable you to obtain clearer ideas on the local action of cold, which forms one subject of this lecture.

In Cook's 'Voyages,' vol. ii., p. 49, you will find the well-known account of the effect of cold in a few hours on Dr. Solander and his companions. He insisted on resting, and "though he had not slept five minutes, he had almost lost the use of his limbs, and the muscles were so shrunk that his shoes fell from his feet." One of his companions could not be made to stir, and the others being too weak to carry him and another a short distance to a fire, they were both found dead in the morning. Dr. Solander was carried to the fire and recovered.

Letellier states that though the energy of combustion in man and the superior animals varies inversely with the temperature of the surrounding air, yet that a fall of one degree of Réaumur causes a decrease of 0·20 per cent. of urea.

Regnault and Réisset found in marmots at a temperature of

A swelling singularly like that of urticaria then occupied, 50° F., 11·2° C., to 72° F., 22° C., that the weight of oxygen consumed per hour per kilo. was =0·085 grm.; when the temperature rose to 93° F., 34° C., the weight of oxygen per hour per kilo. was =0·774 grm. In another scarcely one-thirtieth of the oxygen was consumed while asleep at 44° F., 12° C.

When the body is exposed to a violent shower of water even at 70° F., I found that in the course of four minutes the pulse at the wrist may become imperceptible, and it remained scarcely perceptible as long as the cold water fell on the body. —Brown-Séquard's 'Journal of Physiology,' January, 1858. Chemical action, muscular motion, and nervous sensation gradually become less and less as the cold is continued.

The smaller the individual, that is, the smaller the mass in proportion to the surface, the quicker the chemical actions are stopped, and mechanical congestions of the blood come on. The circle of moving blood becomes smaller and smaller, until the falling temperature reaches the heart itself.

The cold not only stops the chemical changes that occur in the body during life, but it even prevents that peculiar chemical action which begins as soon as fresh oxygen ceases to pass into any part of the body. After death the phenomena of putrefaction first occur in that part of the body in which the temperature is highest. When cold is applied the temperature may be so reduced that even the chemical action of putrefaction may be entirely stopped. The body may remain undecomposed for centuries, and this has actually happened even to so large a mass of matter as exists in a Siberian mammoth.

The general action of cold, then, consists, first, in its stopping chemical action, and this gives rise, secondly, to the mechanical stoppage of the circulation of the blood.

I pass on now to the local action of cold as shown in chilblains and frost-bites. Mr. Simon gives the following experiment: Solid carbonic acid was applied to the skin for five and a-half, sixteen, and forty minutes. It almost instantly became so frozen as to ring like metal. In from fourteen to twenty minutes after the application had ceased the frozen textures had completed their thaw. Blood re-entered them.

but only transiently, the exact area which had been acted on, and was soon lost in a general puffy swelling, which extended for some distance around. With all this the part was entirely without sensibility. Inflammation presently set itself up in the surrounding parts, but the part on which the cold had acted remained without signs of life, and in due time, having suffered no inflammation nor recovered any sensibility, underwent separation as a slough. In other words, all chemical action, all nutrition, all circulation, and all sensation —that is, every kind and sort of motion—is stopped by the excessive cold; and if the freezing temperature could be continued no post-mortem change whatever would take place in the frozen part.

Whatever part is most distant from the centre of the circulation, and presents a large surface for the cold to act on, there local effects of low temperature are most liable to be produced; for example, the fingers, the toes, the ears, and the nose. Between frost-bites and chilblains there is only a difference in the degree of cold applied. Let us shortly consider the most intense effect first. In a frost-bite the degree of cold is sufficient to stop entirely the chemical actions of oxidation and nutrition which are going on in the affected part of the body; all circulation and sensation stops, and this so entirely that no reaction can take place in the obstructed part, and it then becomes a mechanical obstacle to the free passage of blood. This gives rise to increased pressure of the blood in the arteries, and to increased action of the heart, to propel the blood through the obstruction; and this increased action sets up increased oxidation around that part in which all action is stopped, increased heat is produced, and the chemical actions of repair are altered; increased oxidation of non-nitrogenous and of nitrogenous substances, and consequent increased destruction of these substances takes place. If the action continues, adjoining the healthy part increased cell formation occurs. Cells are produced far too rapidly to admit of their healthy change into the textures of the part. The force of nutrition is expended in the production of pus cells, which multiply far beyond the ordinary cell growth of the part.

This action around a frozen part bears the same relation to ordinary inflammation as a motion caused by a push differs from the same motion caused by a pull. In inflammation generally, as in that of the cornea or cartilage, mechanical, chemical, thermal, photal, and electrical motion sets up increased oxidation. The oxidation of non-nitrogenous and nitrogenous matter is accelerated, and this leads to more rapid removal of substance and to more rapid cell formation. Increased molecular motion in the lymph outside the capillaries causes increased mechanical motion of the blood in the capillaries; the vessels dilate, the blood accumulates where there is greatest pressure, more fluid than usual is effused from the capillaries into the surrounding parts, and according to the amount of congestion and the chemical condition of the blood the effused fluid is watery, albuminous, fibrous, or even bloody. The increased flow of blood around the parts where the obstruction by accumulation has taken place, causes increased sensitiveness of the nerves of sensation, and the pressure gives rise to more or less intense pain.

Gradually the increased local oxidation in the lymph outside the blood causes increased oxidation in the blood. This gives rise to an increased amount of fibrin and of its oxides, general increase of temperature is produced, and inflammatory fever disturbing all the circulations, secretions, nutritions, and nerve actions in the body is set up.

In chilblains the action of the cold is usually much less intense than in frost-bites. The primary action, as in the bursting of a lead pipe by cold water, is overlooked, and the results of the reaction constitute the complaint. The cold, instead of stopping entirely the chemical actions in the fingers and toes, so checks the healthy changes that the blood becomes more or less retarded, then congested, and thus the circulation is more or less completely stopped. This gives rise to increased tension in the vessels leading to the obstruction; the impulse of the heart is increased, it urges the blood more strongly forward to overcome the congestion; increased motion of the blood takes place around, increased oxidation is set up, and altered nutrition occurs in and around the

chilblains; thus the healthy action of the part is usually restored, unless the increased oxidation leads to excessive cell formation, then suppuration occurs.

We have then here an example of primary local suboxidation produced by cold, leading to secondary mechanical obstruction, and this mechanical obstruction leads to increased mechanical reaction, by which the proper amount of chemical action in the part is restored.

Thus, in chilblains and frost-bites you are able to see different degrees of the same kind of local suboxidation, both giving rise to the same kind of secondary mechanical obstructions, which must be overcome by pressure and peroxidation before the parts can return to a healthy state.

The second illustration of local suboxidation which I desire to bring before you is fatty degeneration.

A glance at the following table of fatty acids will be sufficient to show you that there are a multitude of fatty substances each differing from the substance below it in the table by containing less oxygen; so that if the first fatty acid was subjected to a process of deoxidation, as in vegetables, it would gradually pass down to the last acid, which contains least oxygen; whilst if the lowest acid were subjected to a process of oxidation, it would gradually pass into formic or carbonic acid.

Monatomic Fatty Acids.

Formic	$C H_2 O_2$,	or 21 Formic $C_{21}H_{42}O_{42}$
Acetic	$C_2 H_4 O_2$	
Propionic	$C_3 H_6 O_2$,	or 7 Propionic $C_{21}H_{42}O_{14}$
Butyric	$C_4 H_8 O_2$	
Valeric	$C_5H_{10}O_2$	
Caproic	$C_6 H_{12}O_2$	
Enanthoic	$C_7 H_{14}C_2$,	or 3 Enanthoic $C_{21}H_{42}O_6$
Thetic	$C_8 H_{16}O_2$	
Pelargic	$C_9 H_{18}O_2$	
Rutic	$C_{10}H_{20}O_2$	
Enodic	$C_{11}H_{22}O_2$	
Lauric	$C_{12}H_{24}O_2$	
Cocinic	$C_{13}H_{26}O_2$	
Myristic	$C_{14}H_{28}O_2$,	or $1\frac{1}{2}$ Myristic $C_{21}H_{42}O_3$
Benic	$C_{15}H_{30}O_2$	
Palmitic	$C_{16}H_{32}C_2$	
Margaric	$C_{17}H_{34}O_2$	

animals with sulphuric acid when the corrosion in the stomach or duodenum was greatest. Hence, in those that died quickest, the fatty degeneration was most apparent. In the cases of poisoning by sulphuric acid, the fatty metamorphosis was most evident in a patient who lived only three hours, in another who lived thirty-five, and in a third thirty-six hours. Sulphuric and nitric acid corrugate, contract, and destroy the blood-globules; the oxalic, tartaric, and arsenic acid dissolve the globules. All these acids cause very similar symptoms—viz., diminished power of the heart, the muscles, and the nerves, arising from the stoppage of the actions of nutrition and oxidation in the organs in consequence of the partial or total destruction of the function of the blood-globules.

It is a certain fact that in organs deprived of the flow of red blood, fatty metamorphosis of the textures occurs. This action may be seen in the neighbourhood of embolism of the vessels and in thrombosis of the arteries of the brain; in the neighbourhood of embolism of the arteries of the spleen and kidney, and even in that of the coronary artery. Experimentally it may be caused at will in the kidney by tying the artery or the vein. In all these cases, fatty metamorphosis quickly occurs.

Traube, with the help of the kymographion, has shown that salts of the bile acids injected into the jugular vein are carried to the right heart, and through the coronary arteries into the capillaries of the muscular structure. The red blood-globules are changed in their structure, or destroyed so that they could not carry the charge of gas which the blood-globules generally contain, and hence the normal amount of oxygen could not act on the muscular substance.

The sinking of the temperature after the injection of phosphoric acid is another evidence of the action on the blood-globules by which the change of matter (oxidation) is lessened. Of all muscles, the heart does most work, and therefore it shows most the effect of unoxygenated blood acting on its muscular fibres.

In the kidneys and liver, the same retardation of the changes of nutrition and oxidation, in consequence of the

injured and dissolved blood-globules, produces the same altered condition of the epithelium and other structures, if death does not occur before the accumulation of fatty matter takes place.

Dr. Pavey, on 'Diabetes,' p. 82, says:—"The introduction of an acid into the system, so as to alter the natural quality of the blood, I have found to produce saccharine urine. This effect has followed the injection of phosphoric acid into the general venous system, and also its introduction into the intestinal canal."

If I had devised a series of experiments for the purpose of proving the existence of local suboxidations in the body, the evidence must have fallen far short of that which these researches on the action of acids offer to you.

Moreover, in addition to the stoppage of oxidizing action in consequence of the destruction of the oxygeniferous blood-globules, there is another action of the acid which, probably, is concerned in determining the production of fat in the kidneys. In the second part of the 'Philosophical Transactions' for 1849, I have shown that when sulphuric acid in large doses is taken, it cannot be proved to pass into the urine, but tartaric acid gives very distinct evidence of its passage; and this confirms the generally-received opinion that vegetable acids do pass so rapidly from the stomach to the kidneys, that a portion of the acid is unneutralized when it escapes into the urine; but another and a considerable portion of the vegetable acid and all the mineral acid must combine with the alkali of the blood, and must make this less alkaline than it was before the introduction of the acid; and the liquor sanguinis being made less alkaline, the immediate effect must be that the lymph in all the textures must be made less alkaline, and thus a check must be given to all the oxidation that takes place outside the blood-vessels; and in the case of vegetable acids this must occur to the greatest extent in the secreting structure of the kidneys, in which, for a time, no free alkali at all may be present, and hence the products of suboxidation should most readily appear in the kidney.

There is another part of the body in which the three conditions on which the production of fat depends are very likely to occur. This is the liver; for, first, an excess of non-nitrogenous oxidizable matter is always present there; secondly, the least oxygenated blood goes there; and, thirdly, the circulation necessary for promoting the action of oxygen on the nitrogenous matter is least there also.

I need only to remind you that the liver is supplied directly with saccharine and fatty matter from the food; that it contains an amyloid substance derived from albuminous substances; that cholesterine and the fatty acids of the bile are evidences of the small action of oxygen in its structure; that no blood is so deoxidized as that which enters the liver, having already parted with oxygen and absorbed carbonic acid in the systemic capillaries; and lastly, that the blood going to the liver has lost nearly all its pressure, and consequently moves at a rate which in the lowest degree promotes the action of the oxygen on the substances in contact with it.

If the different organs and textures of the body were arranged in a series according to the different amount of fat-producing or fat-depositing action that takes place in each, the liver would occupy the highest place and the lung the lowest. The order of the series would vary with the exercise taken, the age reached, the accidents or inflammations that affect the circulation. Whatever increases the circulation in any part lessens the fatty deposition, and whatever retards the circulation diminishes the oxidation, and thereby increases the tendency to the deposition or production of fat.

No perfectly accurate separation can be made between fatty deposit and fatty production, or so-called degeneration. It has been said that wherever the microscopic appearance of fat is greatest *around* the cells or fibres of any structure or organ, there the fat proceeds from deposit, and that where the appearance of fat is greatest *in* the fibres or cells there it is caused by degeneration, in consequence of imperfect oxidation and imperfect removal of the albuminous structures of the tissues or cells. But it must not be forgotten that the same cause may be in action at the same time both within and without

the textures, and that the imperfect oxidation which allows the deposit of fat to accumulate may, in consequence of the pressure thus occasioned, soon increase, so that fatty production may quickly come on; and this may so interfere with the nutrition of the blood-vessels or muscles, that they may become mechanically unequal to the resistance of the pressure of the blood; and thus mechanical apoplexy, or mechanical rupture of the heart, or mechanical albuminuria, may be produced by this primary chemical complaint.

PART III.

ON GENERAL AND LOCAL CHEMICAL DISORDERS ARISING FROM PEROXIDATION, AND ON THE MECHANICAL DERANGEMENTS THEY PRODUCE.

LECTURE X.

ON GENERAL AND LOCAL INFLAMMATION.

Hitherto in these lectures I have dwelt almost entirely on some of the diseases resulting from suboxidation; I shall endeavour now to give you a glimpse of some of those that proceed from peroxidation.

Among the multitude of disorders which may be included under the head of acute and chronic diseases of peroxidation, it becomes necessary for this course of lectures that I should choose only one or two subjects which appear to me most convincingly to prove that an excess of chemical action does originate some of the most serious diseases to which the body is liable, and that this first chemical wrong action sets up mechanical derangements which again become the secondary causes of further more or less serious chemical errors.

In this and the following lecture I shall endeavour to show you that inflammation is a chemical disease, a state of oxidation beyond that which occurs in health, varying in its mechanical results in consequence of the structure of the different textures in which the excessive action is set up.

Hitherto, altered vascular, and more lately altered nervous action have been considered as lying at the root of inflammatory action. These views are based upon the effect produced by section or paralysis of the nerves of the blood-vessels in increasing the circulation through any part, and on the phenomena which result from the obliteration of one artery going

to any part, whereby an increased pressure and action of the blood in other arteries of the part are produced. When, however, the simplest possible case of inflammation is taken in parts where neither blood-vessels nor nerves exist, then we find that there is a chemical action which is independent and anterior to both the nervous and the vascular action; and to trace this excessive oxidation as it arises from physical and chemical action, and as it affects nutrition, circulation, motion, and sensation, is my present object.

No question lies nearer the foundation of all pathological knowledge than that of the nature of inflammation. That it is closely related to the natural actions going on in the body is now fully recognized. Thus, it has been stated to be "a modification of nutrition," "a destruction of the equilibrium in the molecular attractions in the body and of the reciprocal changes between the textures and the blood." But these expressions are dark and fruitless compared with the clearness you will obtain if I can convince you that inflammation in its first origin usually is an exaggeration or excess of the ordinary oxidizing action that occurs in each part of the body, and that this increased chemical action sets up secondary mechanical derangements, which react on the chemical repair of the textures in which the inflammation is set up.

The law of the conservation of energy must be applied to the heat produced in inflammation as it is applied to any other question regarding heat. We have ceased to look for the cause of the ordinary heat of the body in vital or nervous action. We look further, and see it coming from part of the amount of force set free by the action of oxygen in the body, a definite amount of the total chemical force giving a definite amount of heat. In inflammation we must look to the same source for the heat. It is no solution to say that the heat comes from increased vital, nervous, or vascular action, and that these arise from the effect of some stimulus. If it be not fresh created, the increased heat must ultimately come from the force that exists in oxygen, hydrogen, and carbon; and it is more reasonable to refer the heat of inflammation directly to the same source as the ordinary heat of the body,

thereby making the healthy and inflammatory heat proceed from the same kind although from different amounts of the same chemical action, than to attribute the ordinary heat to chemical action whilst the extraordinary heat is supposed to be derived from some other and far less determined source, which itself must ultimately be traced to its origin in the slow combustion that never stops within.

The most simple case of inflammation that occurs in the body will best show you what takes place in more complicated organs. The single fact that inflammation can be set up in the cornea or cartilage, where neither blood nor nerves exist, by increased friction, or heat, or light, or electricity, or by chemical irritants, as cantharides, turpentine, and other oils, or by irritating acids or strong alkalies, is sufficient proof that inflammation does not absolutely depend on nervous or vascular action, but that it may be caused by increased molecular motion. Heat and light and electricity and chemical actions are forms of molecular motion which, when added to the motion already existing in the cornea or cartilage, give rise to increased oxidation of the non-nitrogenous and nitrogenous substance, even in the bloodless textures; and this altered oxidation immediately determines an altered chemical circulation of lymph and an altered nutrition in the inflamed part.

That oxidation takes place where there is no blood-circulation is shown in an experiment on the respiration in the muscles of the frog by G. Liebig. The muscles, even when they were deprived of all their blood, if placed in oxygen, gave rise to carbonic acid and retained their power of contraction.

The increased molecular motion in the cells of the cartilage produces increased chemical circulation of lymph, increased consumption of oxygen, increased liberation of heat and of oxidized products, and ultimately of water and carbonic acid. This action spreads from cell to cell until it reaches the capillaries.

A capillary in ordinary action contains blood-globules loaded with oxygen in its centre, with liquor sanguinis moistening the tube around. Oxygen diffuses from it with the lymph into the cells and structures, and thereby active oxidation is

kept up outside the capillaries in and around the different parts of the different textures. The peroxidation which constitutes the first step of inflammation begins outside the capillaries where the animal heat is produced.

When the increased action reaches the capillaries, the oxygen bearers are, by the demand for oxygen, attracted in excess: they displace the liquor sanguinis—at first producing a more rapid flow through the part, and quickly rushing in, so as to cause a heaping up of the blood-globules, giving rise, first to enlargement of the vessels, and then to obstruction, which immediately reacts on the heart, increasing the pressure and rate of the blood in all the arteries, among others, in those around the obstructed part, so that stronger motion of the blood occurs around the obstruction, and thus a larger area of increased chemical action tends continually to be produced.

That the first mechanical congestions can be caused by increased chemical actions, and not by any nervous action affecting the heart or capillaries, is proved by the fact that when the circulation is arrested by a ligature in the frog, and then irritating substances are applied below the ligature, the blood is seen to be attracted to the irritated capillaries, which will remain congested after the circulation is re-established by removing the ligature.

In the obstructed part the mechanical results of over-fulness and pressure show themselves. The pressure causes pain, and the increased supply of blood makes the nerves around the obstruction more sensitive than when less blood is there.

The tension causes the serum to be effused, and even fibrin, altered by the peroxidizing action going on, also exudes when the pressure increases; and this fibrinous exudation causes intestinal thickening, and constitutes a much more permanent obstruction than the liquid matter, which can rapidly be reabsorbed.

When the primary increase of chemical action is excessive the whole blood participates in it. Peroxidation not only causes an excess of fibrin, but it produces a higher state of oxidation of the fibrin than exists in health. The membrane of the blood-globules also probably is altered in composition

and becomes more adhesive, so that the blood-globules aggregate together and fall more quickly when the blood is drawn from the body, whilst the altered fibrin contracts more firmly than ordinary fibrin usually does.

Oxidation and pressure cannot be increased in any part of the body without the chemical and formative actions of nutrition being at the same time altered. The destruction of old substance will be more or less increased, and the deposit and formation of new substance will undergo great changes, according to the heat that is present, and according to the different textures of the parts in which the increased actions are going on.

The cellular tissue furnishes perhaps the best example of altered nutrition during inflammation. There the increased action most rapidly leads to excessive cell-growth; pus-cells soon form and quickly multiply, according to the amount of increased action. The cell-growth spreads in that direction in which there is least resistance until the products of the altered nutrition are discharged.

When the obstruction is extreme and the pressure excessive in any part of the cellular tissue, oxidation and nutrition may be entirely stopped, and, though excessive action may be going on around, the part obstructed may die, and in it an entirely different sort of chemical action will then be set up, which will continue until the slough is removed.

If, then, in a few words, I try to give you a summary of what inflammation is, I say that it has its origin in the causes which produce the natural heat of the body. The oxidation rises to a peroxidation; it is a purely chemical wrong, producing almost immediately a secondary mechanical derangement—increased motion of the blood-globules—from which excessive motion an obstruction of the blood-vessels arises. Hence proceed increased tension, increased pressure, and increased effusion of lymph from the liquor sanguinis. The effused fluid varies in its composition with the amount of pressure and oxidation. Lastly, from the increased heat and the increased circulation and the increased effusion of lymph, an entire change in the nutrition of the part follows; and

these actions are so related, and so react the one on the other, that it is difficult exactly to estimate the part which each one separately plays in producing the result.

In whatever part or texture of the body the inflammation is set up, the structure of the part will have an important effect on the chemical and mechanical actions that take place in it. Peroxidation will occur much less readily in the liver than in the lung. A resisting bone will oppose a much greater obstacle to congestion than an unresisting skin. Even in different textures of the same organ, the inflammatory action will be modified by the greater or less resistance of the different textures to oxidation and pressure. The inflammation of the outer unyielding covering of the lung will differ entirely from inflammation of the yielding mucous membrane of the bronchial tubes; and the finer structure of the air-vesicles, and of the capillaries on their surfaces, will give rise to very different results from the inflammation of the coarser mucous membrane. Let me for a moment contrast bronchitis with pneumonia.

The increased oxidation in the mucous membrane causes increased fulness of vessels, increased secretion of fluid containing modified albumen and salts, which wash off the epithelium; increased production of the lowest epithelial cells; interference with the passage of air to the air-vesicles. Gradual interstitial thickening of the tubes by fibrin, and even increased growth of the muscular coat, when there is continued cough, may occur. In other words, the structure of the mucous membrane of the bronchial tube, and even its muscular and fibrous textures, determine to a greater or less degree the products and the results of the bronchitis.

In the air-vesicles, no epithelium, no muscular coat exists; the oxidation causes congestion of the capillaries; thence comes an exudation of blood-stained albuminous liquid, and the rapid effusion of oxidized fibrin into the vesicles. In the effused substance and in the obstructed capillaries further chemical changes and altered nutrition then occur, whilst the mechanical obstruction, according to its extent, limits and retards the great chemical action which is going on between the oxygen of the air and the red globules of the blood.

The same chemical stoppage of aëration of the blood follows, not more surely, but much more manifestly, from mechanical action by an accumulation of fluid in the pleura. The structure of this tissue determines the effusion of altered serum and fibrin whenever excess of oxidation causes congestion of the capillaries. The amount of fluid and solid matter effused depends on the amount of obstruction of the capillaries, and the pressure is transferred to the surface of the lung; and, as it increases, the chemical action in the lung is lessened until so little oxygen passes into the air-vesicles that extreme suboxidation ends in stopping all the actions that constitute life.

In order, however, to bring before you still more clearly the dependence of mechanical on chemical diseases, and the alteration of chemical function by the alteration of mechanical structure, I shall occupy your attention in this and in the following lecture with those different structural affections which, under the name of Bright's disease, have so united chemistry to medicine that, as regards this disease at least, no one can even now say that it is possible to be too chemical. For only by chemistry can the disease be recognized, only by chemistry can its progress be traced, only by chemistry can the effect of the different poisonous substances retained in the blood and in the textures by the stoppage of their chief means of escape be comprehended, and only by chemistry can the actions of the different means of promoting recovery be understood.

In the cortical part of the kidney, as elsewhere, the structure of the various textures determines the effect of the chemical and mechanical actions that take place within them. Shortly, omitting the tubes of Henle, it may be said that the kidney consists of cell-tubes united by connective tissue covered outside with capillaries, with an arterial tuft inside the closed end of the tubes. Hence it may be said that the cortical structure is composed of three different textures—first, blood-vessels with malpighian tufts; secondly, connective tissue, including the capsule of the kidney; and, thirdly, urinary tubes with epithelium and basement membrane.

Professor Ludwig has called the kidney a hydraulic press, formed to produce that amount of pressure which is required to cause a flow of urine to take place. Before we enter on the effect produced by altered oxidation and nutrition in the different components of the cortical structure, it is very desirable that the effect produced by altering the pressure in the veins and arteries should be clearly set forth. Multitudes of experiments have been made by different observers on ligatures of the renal vein and artery. When the renal vein is tied, the kidney swells in every part with blood to twice or thrice its ordinary size. In an hour or two blood is poured out between the renal capsule and the cortical structure. Afterwards the tufts break and blood escapes into the tubes. The urine is albuminous from the commencement, with blood-globules and excess of epithelium, and if the animal does not die before changes of nutrition occur, the epithelium of the tubes is seen to be thickened, and fatty deposit to have taken place.

When the renal artery is tied, the circulation is partly kept up by the smaller arteries; but the pressure is not sufficient to drive the blood through the capillaries. Hence stoppage takes place in the veins. In a few minutes the medullary substance seems full of blood, whilst the malpighian tufts are collapsed. In two or three hours, from venous congestion, the kidney attains its former size. After twenty-four hours it begins again to decrease, and the longer life lasts the smaller it becomes. In two or three days the renal capsule becomes thickened and adherent. The urine is scanty, with albumen, epithelium and blood-globules and fibrinous cylinders. In from seven to more hours the epithelium in the tubes is seen to be thickened, and in twenty-four hours there is fatty matter present in excess, and this increases until the epithelium cells are entirely destroyed. The renal vein may get stopped with coagulated blood, and abscesses may form in the cortical structure and pus-cells may be seen in the tubes. In from one to three weeks there are still more marked errors of oxidation and nutrition. Very thickened renal capsule. Larger abscesses. Indistinct tufts. Tubes full of fatty matter, and the connective tissue thickened.

Attempts have been made to study the effects of pressure when, after removing one kidney, the abdominal aorta has been tied below the renal artery of the other kidney, so as to throw the greatest pressure of the blood on this kidney, but the operation does not allow of any dependable deductions. Far more may be learnt as to the effect on the urine by studying the alterations of pressure caused by different diseases.

Thus, whatever increases the action of the left ventricle, producing increased tension of the pulse, increases the arterial pressure on the tufts, and if sufficiently strong, produces a congestion, giving rise to albumen or even blood-globules in the urine.

The same result may follow from causes that excessively depress the action of the left ventricle, or so diminish the tension in the renal artery that stoppage in the renal vein takes place. Thus pericarditis, with much exudation, extreme thickening of the aortic valves, or thickening and insufficiency of the mitral valve when no compensation for the weakened circulation is caused by hypertrophy and dilatation; aneurism or disease of aorta. All these diseases may produce an effect resembling in kind that produced by tying the renal artery. Diseases of the heart with insufficiency of the tricuspid valves; diseases of the lungs, with great difficulty of breathing, as pneumonia, pleurisy, emphysema, tubercles in excess, and all diseases that so depress the energy of the heart that the blood stops in the veins, as at the end of typhus fever, carcinoma, tubercle, these all produce effects resembling those produced by tying the renal vein.

Within small limits a certain pressure of blood in the tufts determines the passage of water into the tubes; increased pressure causes increased flow of blood through the kidneys, and produces increased secretion; but excessive pressure or very diminished pressure loads the vessels of the kidney and stops secretion, and if continued, ruptures the malpighian tufts, or causes albumen to exude.

The total quantity of dry albumen which passed out in twenty-four hours in the urine in different states of Bright's

disease was found to vary from a few grains to at most about one ounce, a loss of no serious import.

Having thus brought before you the effect of variations of mechanical pressure in altering the chemical condition of the urine, I shall now try to show you how altered chemical actions in different textures of the kidneys may give rise to altered mechanical conditions, as well as to altered states of nutrition and altered chemistry of the urine.

In Bright's disease very different chemical and mechanical results are produced when the different structures of the kidney from any cause take on a more active state of oxidation than occurs in the state of health.

It must be remembered that it is not yet forty years since Dr. Bright first drew attention to this complaint. Since then, though much confusion and misinterpretation has from time to time arisen, yet the progress of sound knowledge has been rapid, and a few years more will find all the difficulties and uncertainties regarding Bright's disease entirely removed.

Here, instead of confusing you with fatty disease, amyloid or fibrinoid disease, diffuse nephritis, parenchymatous nephritis, desquamative nephritis, and a multitude of other names, I shall try to point out the different results of peroxidation of the arteries, of the matrix, and of the tubes. As in inflammation of the lungs, whilst distinctly separating inflammations of different structures, I by no means meant that pleurisy and pneumonia, or bronchitis and pneumonia, or all three inflammations, cannot occur at the same time, so in inflammation of the kidney, interstitial nephritis and the so-called amyloid or fibrinoid disease, or interstitial nephritis and tubular or so-called desquamative nephritis, may occur at the same time; although, for clearness, I shall shortly bring before you each of these inflammations and their results separately.

In inflammation of the cortical structure of the kidney, it must be remembered that every possible degree of intensity or mildness, every possible variety of complication or of simplicity of textural affection, may occur; and although here, as elsewhere, a stage of increased action, a stage of effusion, and a stage of absorption may occur, yet anywhere a more or less

permanent halt may take place, or the increased action may recommence with an intensity and extension beyond that of the original complaint.

Though I am well aware that amyloid or fibrinoid disease is called a degeneration, and not an inflammation, yet I am sure that these undefined terms will come to represent the separate or consecutive action of different degrees of peroxidation and suboxidation, and their mechanical and chemical results. I shall therefore here treat of fibrinoid disease as arising from an increased action consequent on increased pressure and increased chemical change in the textures of which the artery is composed. From the action of iodine and sulphuric acid on the deposit which occurs in the arteries of the kidney, Virchow concluded that a peculiar starchy deposit took place, and that this gave rise to one form of disease which was included under the general head of Bright's disease. There can be no question that starch granules are produced in the prostate and elsewhere, and there can be no doubt that starch, sometimes in considerable microscopic quantity, does occur in the urine of women and men. The granules of starch in urine passed with every care to avoid external starch, become immediately blue with iodine. They swell up and disappear when treated with strong acid; give rise even to sugar when treated with saliva; but in most of the cases that I have seen there has been no albumen in the urine, nor any former history of any symptoms resembling Bright's disease, nor, even though the cases have been closely watched for months, have any symptoms of Bright's disease come on. Moreover, Virchow's so-called amyloid deposit has nothing to do with starch, except the name, which must be changed. It contains 15 per cent. of nitrogen and 53 per cent. of carbon; and in Virchow's 'Archives,' vol. xvi., p. 50, Frerichs states probably its true composition—that it is an altered fibrinous deposit. It is probably the result of an oxidizing action on fibrin effused into the muscular texture of the artery. The action begins in the walls of the smallest arteries, and extends from the malpighian tufts even to the renal artery. In extreme cases of contracted cortical structure, the diameter of the vessels is so narrowed

that water even will hardly pass. Dr. Dickinson found, in some experiments made at my suggestion, that a pressure which sent 119 ounces of warm water through the healthy kidney in ten minutes, through a very contracted kidney caused less than five ounces (4℥ 6ʒ) to pass in the same time.*

I have already just now described to you what happens when the renal artery is tied and blood in very small quantity is able to pass into the cortical structure. The first result was immediate alteration in the chemistry of secretion, and the second result was an entire change in the chemistry of nutrition of the organ.

In the much slower process of general obstruction consequent upon thickening from slow peroxidation and increased pressure in the walls of the artery, the same two great results are produced.

First, the effect appears in the altered chemistry of secretion.

The quantity of water that can pass through the vessels of the kidney after death, although it gives no certain measure of the quantity of urine the kidney can secrete during life, yet gives some clue to the quantity of blood that can pass through the malpighian tufts to the capillaries from which the solid constituents which make up the contents of the urine are probably chiefly separated.

Gradually, as the arteries and malpighian tufts become thicker, the course of the blood is thrown on the vascular circulation in the mammary portion of the kidney, and large quantities of water with but little of the proper constituents of the urine may there escape. But for this, the result on the secretion by the cortical structure would very quickly be the same as follows from tying the arteries that supply the kidney. The effects produced by tying the ureters have more resemblance to those produced by obstruction of the urinary tubes.

The latest experiments prove that the cortical structure of the kidneys must not be considered simply as diffusion tubes,

* 'Med. Ch. Trans.,' vol. xliii., p. 243.

with blood pressure on one side of the membrane and air pressure only on the other.

In the passage of muscle, nerve, cellular, and other highly-complex substances out of the body, we must remember that long and various series of products are formed, many of which are still unknown. Between the time when these complex organic compounds begin to leave the textures until they are finally thrown out by the kidneys and skin as they pass on through the lymphatics, blood, and excreting organs, they undergo continual downward change of composition by oxidation.

Thus, in the textures, one part of the albumen, fibrin, or syntonin, &c., may be oxidized, and give rise to highly-complex neutral and alkaloid substances, and a part of these new substances even there may pass into substances as low in the series as kreatin, and a part of these may pass into uric acid or even into urea, whilst the largest part of the kreatin substances will pass into the blood, and a part of these will there be oxidized to uric acid, or still lower, whilst the larger portion will go to the kidney and skin, and there give rise to substances like uric acid, and sudoric acid, and urea; and when the action in the last oxidizing place is complete, urea, carbonic acid and water alone may be the final result.

Thus, the following sketch may be made:—

Albumen, fibrin, syntonin, &c., &c.
Highly-complex neutral and alkaloid substances.
Substances having at least as much carbon as kreatin.
Substances as far down as uric acid.
Urea.

In the textures. In the blood. In the urine and skin.

The urea may undergo another chemical change anywhere in or out of the body, and give rise to carbonate of ammonia.

Removal or suppression of the passage through the arteries of the cortical structure stops the higher compounds from passing to the kidney to undergo changes there; whilst tying the ureter or stopping the tubes causes the urates and urea to be reabsorbed back into the blood. The different states of altered chemistry of the blood, lymph, and textures thus produced have all been included in one general term—uræmia;

and as this may arise from thickened vessels, thickened interstitial texture, or thickened tubes, and as it is a most remarkable example of secondary chemical disease arising from a mechanical obstruction caused by a primary peroxidation, it will form just one of those illustrations of the relationship of chemical to mechanical and mechanical to chemical disease which I have endeavoured in this course of lectures to bring before you.

The first theory of uræmia came from Dr. Wilson, at St. George's Hospital ('Med. Gaz.,' 1833, on "Fits and Sudden Death in connection with Diseased Kidney"). He attributed the symptoms to diminished albumen and excess of urea in the blood,—the discovery of Bostock and Christison. In 1851, from very careful experiments, Frerichs came to the conclusion that urea was not the poison, but that it gave rise to carbonate of ammonia, and that the symptoms depended on ammoniæmia.

Schotten found in uræmia the proportion of extractive matter to albumen in the blood increased from 5 : 100 to 40 : 100, and Hoppe found the kreatin five times more than in healthy blood.

Traube thinks uræmia does not proceed from any definite poison or poisons, but from œdema and anæmia of the brain. If the anterior lobes are affected, this causes coma; if the middle lobes, coma and convulsions. Variations of arterial pressure give rise to the œdema, and this to the anæmia.

Multitudes of experiments have been made on animals in support or in opposition to these different views. I shall only have time here to bring before you the last and best experiments, premising that Oppler, in Virchow's 'Archiv.' vol. xxi., p. 260, was the first to observe that after tying the ureters the urea in the blood was much more than after extirpation of the kidneys, and hence he concluded that part of the urea in the urine was formed from some other substance in the kidney. He also determined the amount of kreatin in healthy muscles, and found that one kilogramme of muscle gave one-third of a gramme of kreatin. After nephrotomy (forty to fifty hours) he obtained from the same weight of flesh 2·2 grammes of kreatin.

Dr. Zalesky, in Hoppe's laboratory, has carried on a long nvestigation on this subject, more especially on animals that do not in health produce urea, but stop at the formation of urate of ammonia. He found that when one kidney was left, or when one ureter was pervious, symptoms of wrong chemistry hardly occur, but when both kidneys in snakes were removed, or both ureters were tied, death was caused twice as quickly by the former injury, and the chemical results were entirely different in the two operations.

When the ureters in birds were tied they continued to produce urates, and these are reabsorbed and deposited first in the lymphatics, and secondly in the joints, coating them as thoroughly as the most gouty joint is coated. The urates, moreover, covered as with white paint the liver, the pericardium over the heart, the peritoneum in places; even in the substance of the heart, and under the endocardium of the valves, and on the sides of the papillary muscles urates were seen; out of the ducts of the stomach-tubes little casts of urates could be squeezed by gentle pressure, and even in the aqueous humour of the eye urates were found.

When the ureters of snakes were tied, death occurred twenty-nine days after the operation. The œsophagus, stomach, and bowels contained urates. The surface of the liver was mottled with urates. In the structure of the spleen, the outer surface of the kidney, and the surrounding parts, urates were found, and all over the surface of the different organs and the bowels the deep white colour of the urates were seen, and uric acid was detected in the aqueous humour of the eye. When the kidneys were entirely removed, the animals died fourteen or fifteen days after the operation. No uric acid was then found in the muscles, liver, or lungs, and a mere trace occurred in the bowels.

Dr. Zalesky made a series of experiments on the amount of urea in the blood, muscles, and other parts of dogs in health, and in the same parts when the kidneys had been removed, and when the ureters had been tied. Taking the average of his experiments—

	In health.	When kidneys were removed.	When ureters were tied.
In blood per cent. of urea .	·00396	·0016	·0523
In muscle „ „ .	·00171	·0020	·0418

Neither in birds nor in mammalia could any marked increase of ammonia in the blood be found after the ureters were tied, nor after the kidneys were removed. Thus

Carbonate of ammonia.	In health.	When kidneys were removed.	When ureters were tied.
In 100 grammes of blood of birds	·0058 gr.	—	·0069
„ 100 „ „ dogs.	·0029	·0096	·0070

Dr. Zalesky concludes that Frerichs' theory of ammonia poisoning must be given up, and that as uræmia occurs in animals that never form urea, and as there is more urea in the blood when the ureters are tied than when the kidneys are removed, though the uræmic symptoms occur at least quite as quickly after the last operation, so the urea theory cannot be maintained. He considers Traube's theory of the excess of water and pressure unproved, and he thinks Oppler's experiments point to the want of separation of other substances besides urea and uric acid as the cause of uræmia.

	Grammes per cent.
In mammalia he found that the average amount of kreatin in healthy muscles was	·060
„ „ when the ureters were tied .	·280
„ „ when the kidneys were removed	·351

It is in the highest degree probable that as in different plants under variations of structure, growth, deoxidation, and climate various combinations of elements are synthetically built up into different alkaloids, so in different parts of animals variations of structure, growth, oxidation, and temperature may analytically form out of albuminous substances even the same or more highly carbonaceous alkaloids, or neutral or acid substances, which ultimately pass down through kreatin and kreatinine to uric acid, urea, and carbonate of ammonia. Among these higher compounds one or more substances may be formed or retained in excess which by direct chemical contact with the nerves and muscles may give

rise to symptoms resembling those produced even by morphia or strychnia.

The experiments of Dr. Zalesky prove that urates are deposited on the non-vascular cartilages and in the aqueous humour of the eye when the ureters of birds are tied, and this confirms the results I have published in the 'Proceedings of the Royal Society,' vol. xiv., p. 400, that soluble substances as quickly as they go into the blood pass out of it into every organ and structure of the body. When urea, urates, or any other substance exists in excess in the blood, it must at the same time exist in excess in every vascular and non-vascular structure of the body.

The second result of obstruction of the arteries is shown in the altered chemistry of nutrition of the kidney.

I have already brought the result of this before you in this lecture when speaking of the fatty deposit which in a few hours results from ligature of the renal artery. What happens in a few hours in the experiment happens more slowly, but not less surely, in this disease of the kidney. The structure not only wastes from insufficient supply of blood, but long previously, from insufficient supply of oxygen, there is an accumulation, if not a production, of fat everywhere.

As the disease continues the cortical structure becomes less and less nourished, and the deposit of fat increases. The fatty deposit is not the cause of the wasting, but the obstruction causes the wasting and the fatty deposit and fatty production; although when these are in excess they react on the circulation through the vessels, and by increased pressure tend to make secretion and nutrition more difficult.

But you must not suppose that an acute or chronic alteration of the chemical, mechanical, and nutritive actions in the coats of an artery can occur without the action extending to neighbouring or even distant textures.

The nearest texture in locality is the interstitial cellular texture of the kidney; this takes on the same increased chemical action and the same altered nutrition, and even the neighbouring tubes may participate in the increased action and modify the symptoms and accelerate the progress of the

complaint. These diseases must form the subject of my next lecture. Here, however, I must point out to you a fact arising from the equality of the pressure of the blood in the arteries. In the whole arterial system—from the heart to the capillaries, omitting the gradually increasing friction—the pressure at any one moment is always the same throughout every part. A rapid or gradual increase of pressure in any part implies an increase of pressure in every other part; so that much pressure in the small arteries in one point produces pressure everywhere, and this increased pressure gives rise to altered chemical action in other small arteries. Hence the increased resistance in the kidney causes increased pressure in other arteries and increased action in the left ventricle; and then other small arteries, as in the spleen and the liver, take on the same action and show the same deposit when treated with a solution of iodine in glycerine. Moreover, this uniformity of pressure leads to more or less of this thickening of the small arteries in other states of obstruction of the kidney and in many other diseases; so that disease of the interstitial texture or of the tubes of the lungs, of the liver, of the spleen, of the heart, occur where this fibrinoid disease exists. Vogel states that, taking extreme, partial, and slight cases, amyloid disease is present in the kidneys of half the fatal cases of Bright's disease which he examined. In any chronic disease in which there is obstruction to the arterial circulation, and consequent increase of pressure in the small arteries of the kidney, this increased action and thickening tends to occur.

Dr. Dickinson, in his paper in the 44th vol. of 'Medico-Chirurgical Transactions,' has included diseases of the artery and interstitial texture under one head of granular kidney. The records of 2350 post-mortems in St. George's Hospital in ten years gave 250 with granular kidney; of these, in 43 per cent. there was disease of the valves of the heart; and in 52 per cent. there was atheroma of the arteries, and no less than 17 out of 250 died of sanguinous apoplexy.

In this as in other forms of Bright's disease no special actions of medicines, no specific, can be of benefit. Filling every texture, including the altered texture of the kidney,

with more alkalies, or with less alkali, or with oil, or with salt of any kind, will not remove the thickening. Mercury probably combines with every particle of fibrin in the body, and alters its properties, making it less coagulable and hastening the changes it passes through in its downward progress towards water, carbonic acid, and urea; but when the secreting power of the kidney is lessened, instead of escaping in large part by the kidney from the moment it enters the circulation, it escapes only to a very small degree, and thus it is left in greater quantity to diffuse into the textures, or to attach itself to some texture where it may lie dormant until that texture is redissolved. So that even in this form of Bright's disease mercury may set up an intense oxidation in other parts to which it passes; and therefore here it must be used in very small as well as in rare doses. One exception I have found to this rule, and that was in a case of amyloid disease, where, in consequence of the treatment necessary for dropsy, strong hydragogue cathartics, colocynth, elaterium, croton oil, were taken, and borne for many weeks with great advantage. In this case calomel in grain, or even two-grain, doses was taken each night for weeks, and yet no affection of the gums was seen. By far the largest portion of the mercury probably helped the action of the elaterium that was used; and even of that portion of the mercury that was absorbed probably a part was removed in the watery exudation from the bowels which took place daily.

It might be thought that the action of iodine and alkalies would affect the thickened arteries; but no manifest gain has come from the use of these remedies, and the treatment always ends in giving up medicines that act on the causes and alterations of the disease, and in endeavouring to meet the symptoms and complications as they arise. As these are common to other forms of Bright's disease, I shall postpone what I have to say on the treatment of dropsy and uræmia—the two most important complications—to my next lecture.

Prognosis.—Of all the forms of Bright's disease this seems the one in which, without perfect cure, the longest pauses or stoppages in the progress of the disease are occasionally met

with. It differs much from the affection of the tubes, in which recovery frequently takes place, and in which no trace of albumen is met with in the urine when the disease has passed away. In amyloid disease, probably with cirrhosis of the kidney, I have witnessed for years the albumen continue to be present in the urine, although all the other functions of the body, including the procreation of healthy children, have been well performed. Still, as the disease of the kidneys arises from, or is followed by, affections of so many other organs, the prognosis is generally most unfavourable; and when cirrhosis and tubular affection of the kidney also are present the rate at which the cortical structure disappears may vary extremely in different cases, but usually it goes on surely, until the kidney almost ceases to have any cortical structure at all, and finally the same results follow as if the kidneys had been almost entirely removed.

LECTURE XI.

ON BRIGHT'S DISEASE—*Continued.*

The ordinary oxidation which takes place in each texture of the body gives heat and motion sufficient to carry on the ordinary nutrition of the structure; but the smallest increase of oxidation set up by direct extra-vascular or indirect intra-vascular motion through the nerves is followed by altered heat, motion, and nutrition.

The effect of slow, but continued peroxidation may be watched in the skin or in the eye continually; and within the body mechanical alterations show no less clearly what such increased chemical changes can effect. The slightest long-continued mechanical pressure produces not only thickened cuticle, but altered nutrition of the skin itself; or a slight cut may cause a thickening which may last for months or years after the slight inflammation which united the surfaces has passed away. So in the cornea the most chronic inflammation from some slight mechanical cause will leave a thickening which may be perceptible for years. Or if you look within you may see the most chronic gout, rheumatism, or scrofulous inflammation, when long continued, slowly cause such an amount of thickening in the joints and other parts that the utmost mechanical impediment to motion may ultimately result.

Of all textures the cellular texture is the one in which substances pass most immediately from and to the blood, and in which alterations of oxidation and nutrition are most liable to occur.

In the kidney this cellular tissue constitutes the interstitial structure and the capsule. It is much less developed than in other organs, and it is so related to the vessels and tubes that altered action can hardly be limited to this structure alone.

Still, for clearness, I shall treat of its thickening and cell-

growth under the head of interstitial nephritis. Dr. Dickinson includes this inflammation in his parenchymatous nephritis; but Virchow has defined parenchyma as "the proper structure" of the kidney, including the tubes, with their epithelium and capillary system; so that, though I shall use Dr. Dickinson's observations, I shall not adopt his nomenclature. In the 'Med.-Chir. Trans.,' vol. xliii., p. 235, Dr. Dickinson says:—"It is common to meet with kidneys as to which there is a doubt whether they are healthy or not. The capsule is a little thickened, and it is more adherent than it should be. When removed the surface presents a confused, muddy appearance; and it may be noticed that a thin layer of capsule is adhering to the kidney. As yet there is no distinct granulation, though the tendency may be indicated by one or two curved depressions, or by a little general roughness. On examining such a kidney in section, we shall find all the central parts quite healthy, save that closely attached to the inner capsular film we shall see certain narrow projections insinuating themselves between the tubes. If we observe the position of an external depression or cicatrix, we shall find that from this passes inwards a process of fibrous-looking material, which is seen to involve in its interior the contracted remains of tubes it had embedded in its passage. It looks as if an effusion, small in amount, had commenced in the surface and worked its way inwards among the ducts, numbers of them thus becoming completely surrounded. After a time contraction follows in the wake of the exudation, and the tubes imbedded are reduced to mere microscopic threads. At the same time another result of the contractile tendency appears. The points at which the processes originate become depressed, and when these are numerous and tolerably regularly distributed the result is superficial granulation."

A slight increase of the ordinary oxidation in the cellular tissue leads to increased flow of blood, to increased production of cells and fibrillæ, and, when the chemical action is considerable, to suppuration. After a time the increased pressure from the effusion and thickening causes diminished supply of blood, and hence imperfect nutrition and oxidation, con-

traction, and even fatty deposit are seen in the interstitial texture, and ultimately the nutrition and secretion of the kidneys is visibly affected. The kidney becomes smaller than natural, the capsule very adherent, the surface rough and uneven, the stellated veins distinct, the substance hard; frequently the capsules of the malpighian tufts and the basement membrane of the tubes ultimately are involved in the thickening. Interstitial nephritis and cirrhosis of the liver are similar diseases affecting similar structures. In both the mechanical pressure that is produced stops the chemical function and the nutrition of the organ in which it occurs.

Causes of Interstitial Nephritis.

Every substance that enters the stomach passes into the blood and surrounding textures according to its diffusibility. It is carried by the blood everywhere, and again, according to its diffusibility, it passes into every structure of every organ and into every surface by which it can be thrown out.

In its passage in, during its stay, and in its passage out, it acts according to its chemical affinities for the gases, liquids, and solids with which it comes in contact, and the effects produced vary according to the chemical actions that take place.

If the ordinary substances that daily go in are represented by oxygen, water, salt, bread, meat, and stimulants, none of these except the oxygen have the degree of chemical action which so-called stimulants possess. Setting aside tea and coffee, our stimulants are essentially alcohol; and it is the long-continued strong chemical action of this substance on oxygen, and on the different textures at the temperature of ninety-eight degrees, that gives rise so frequently to that increased motion and increased thickening, followed by contraction and suboxidation, which constitutes cirrhosis of the liver and kidney.

Let me for a moment follow a dose of alcohol through the system. It passes through the stomach, and in going through is to a small extent oxidized. The greater part escapes, and enters the circulation, acting there on the oxygen, fibrin,

albumen, and blood-globules to a small degree. In a few minutes a part passes, whilst still being oxidized, into every secretion, as, for example, into the lungs, kidneys, liver; whilst another part passes into every other texture; and on each substance in each texture the alcohol produces its chemical action, still continually undergoing oxidation, so that in a few hours one part has entirely escaped, and another part has been entirely oxidized in the blood and textures. What has the alcohol during this time done? It has acted chemically on oxygen and on the textures with which it has been in contact. The first action has little to do with the strength of the alcohol. Strong or weak, it combines with oxygen; more or less increased oxidation, increased circulation, increased secretion, increased effusion of liquor sanguinis, and altered nutrition result. The second action depends on the strength of the alcohol. Strong alcohol acts chemically on albumen, fibrin, cellular tissue, &c. It has a powerful attraction for water, and it shrivels up cellular tissue, hardens fibrin, and precipitates albumen by its chemical properties.

To no organs of the body is more alcohol taken than to the kidneys and liver, and in no organs are the mechanical results of its chemical actions more manifest and the consequences of the altered structure more apparent; and the increased oxidation, the increased flow of blood, the altered nutrition are identical in kind with the first actions of inflammation; and when the series of actions are repeated over and over again for years, the result is the same as might have been produced in a shorter time by an ordinary inflammation when no alcohol whatever had been taken.

Dr. Christison states that three-fourths of all the cases of Bright's disease which he saw were produced by the habitual long-continued abuse of drink. Very great occasional excess did not act so strongly as long-continued smaller excess.

No doubt the alcohol acts on the vessels and ducts; but not so powerfully as on the interstitial texture, with which we are at present occupied.

On the Symptoms and Consequences of Interstitial Nephritis.

If the disease could be limited to the interstitial texture, and to that alone, it is possible that no appearance of albumen in the urine might occur. No fibrinous casts might be seen. The kidney might gradually, by its contraction, cease to secrete urinous matter, and uræmia would be the final result. But the affection spreads to the vessels and tubes, and then the pressure in the tufts or ducts is altered and albumen is effused, the production of epithelium is increased, and some fibrinous casts appear in the urine.

Usually the specific weight of the urine becomes less and less, and generally this weight may be taken to be directly proportional to the amount of cortical structure that exists; so that when the specific weight of the urine is least the cortical structure is least also. Even when hardly any cortical structure is left, an excess of water of the lowest specific gravity may be thrown out, most probably from increased circulation in the mammary part of the kidney.

As long as this excessive flow continues no dropsy occurs, and hence throughout the whole course of the disease no dropsy may occur. The altered blood and the altered lymph may give rise to all kinds of hæmorrhages, thickenings, and effusions, and chemical actions on the nerves and muscles, which may be summed up in the word poisoning, and which I have already brought before you when speaking of uræmia.

At any period during the progress of the disease more acute inflammation may suddenly come on, and in the cellular tissue, more readily even than in the tubes, pus-cells are soon formed, suppuration extends throughout the altered cortical structure, and rapidly that assemblage of low feverish general symptoms which now appears to us to be so very inaccurately designated as a typhoid state is produced.

With regard to treatment, medicine avails little for stopping the effect of alcoholic poison or for removing the thickening of the interstitial structure. No appreciable alteration of structure occurs until the alcohol has acted for months; but as each day produces its infinitesimal effect some good may

be done by recognizing the disease early and by stopping as far as possible the further action of the poison. Usually the second nature cannot be changed, and the treatment consists then only in alleviating symptoms and in warding off complications as they arise.

Of all the symptoms that of general debility is the one which will most frequently present itself to you, and of all the complications uræmia is the one which is most serious.

The loss of general mechanical power consequent on wrong chemistry of the blood and lymph begins from the very commencement of the disease, and lasts until its final close.

One of the first effects in the blood is the insufficient production of blood-globules, on which the passage of oxygen into the blood depends. The gradual diminution of albumen in the blood is a very much more remote cause of symptoms, and as long as food can be taken this admits of an easy remedy; whilst the reproduction of blood-globules requires a far more complex chemistry, and necessitates an increased supply of iron for the formation of hematine.

The accumulation of chemically descending substances in the blood, and still more in the lymph which surrounds and permeates each particle of every structure, must begin from the moment that the kidney begins to perform the function of oxidation and excretion imperfectly. Still it is evident from the experiments in which one kidney has been removed and no poisoning has occurred that even half the structure may be destroyed by disease without the occurrence of bad symptoms. This is a large margin for safety, but as soon as this is removed the lymph begins to cause wrong chemistry in the textures. Products of downward change from urea upwards keep circulating in the blood and lymph, and these substances produce their chemical actions everywhere. Thus on each mucous and other membrane urea exudes, and in the mouth even it is converted into carbonate of ammonia, and this, with some urinous-smelling substance, gives the foul breath that is so frequently observed. The same substances effused in the stomach give rise to sickness, and in the bowels often to diarrhœa. The higher uric-acid compounds in the joints produce chronic

gout, and the excess of kreatin in the muscles may stop the changes in the syntonin, whilst the still higher compounds as yet uninsulated may in the nerves and brain produce irritant or narcotic symptoms from the slightest cramp or subsultus to the most profound coma. That there is in every case some distinct local action is clear from the amendment or arrest of the symptoms which is occasionally observed. The sickness and the diarrhœa may be stopped, the convulsions may cease, the coma may disappear.

Let us look at the removal of the poisonous substances a little closer. The vomiting and diarrhœa are not to be checked by strong remedies when the ammoniacal and urinous odour tells you of the accumulation of poisons within. You must, whilst endeavouring to obviate the extreme prostration which these actions cause, remember that more serious muscular and nervous actions are at hand, and that except by acting on the skin, you have no other gate through which the poisonous substances can pass out. Warm baths and hot-air baths give no immediate relief like vomiting and purging. I have been asked by a patient for an emetic when he was within a few moments of his death from exhaustion. Almost whilst speaking to me another violently relaxed action of the bowels came on, and from the effects of this he died.

By the stomach, by the bowels, and by the skin, all poisonous substances can be thrown out of the blood and lymph, and, according to circumstances, by this or that road a passage must be obtained.

Irritative actions of the nervous system seem to mark a less degree of affection of the nerves than narcotic actions, and cramps, subsultus, and epileptiform convulsions pass away or yield to treatment far oftener than oppression and coma.

To any of you who have witnessed the stoppage of convulsions in Bright's disease by the inhalation of chloroform, the thought must have occurred that the chloroform must have so acted directly on the nerve as to render it incapable of being irritated by the urinous poison. A volatile coma, so to say, is produced. Perhaps the local action of the urinous poison is checked by the substance on which it was acting

being altered in composition by the chloroform. But when the urinous poisons are causing both convulsions and coma, then this fixed coma is more dangerous than the convulsions; and all your efforts must be directed to stop the local action on the nerves, and whilst doing your utmost to evacuate the poison, you must try, by counter-irritation, to determine by blisters the largest possible effusion of serum and lymph as near as possible to the spot where the wrong action is taking place.

Causes of Tubular Nephritis.

It is scarcely possible for disease of the arterial and interstitial structure of the kidney to exist without an affection of the tubes. It is far more possible for the tubes to be affected without the interstitial texture participating in it. The malpighian tuft must be considered as part of the tube, and the slightest increased action, pressure, or thickening in the tube must immediately affect its malpighian tuft.

Of all the names that have been given to this form of disease, that of tubular nephritis appears to me the most simple. In its comparative mildness, in its occasional intensity, in its long duration, and in its rapid and perfect cure, it resembles slight, severe, chronic, and rapidly-curable bronchitis. If it were not for the albumen poured out, and for the urinous matters kept in, there would be, as in bronchitis, a peroxidation set up in the tube outside the blood. This would cause increased flow of blood in the vessels, increased formation and shedding of epithelium, increased pressure and thickening from fibrin. Then obstructions would come on, stoppage of the blood, stoppage of oxidation in the most obstructed part, and production and deposit of fat, and alteration of the composition of the nitrogenous texture by the stoppage of nutrition, whilst around the obstruction a widening circle of increased action would exist.

Of all the causes that affect the tubes of the kidney cold is the most striking.

The sudden stoppage of the removal by the skin of water, salts, lactic and hidrotic acids, urea, and probably a multitude

of other substances, immediately causes an accumulation of these or their parent substances in the blood. No sooner does this occur than on every mucous membrane and in the lymph that diffuses into every structure these substances are poured out. The greater part of the skin excretion must temporarily pass off by the kidneys or bowels. Hence increased chemical and mechanical action, increased flow of blood, increased oxidation, and, if this becomes excessive, obstruction occurs; then follow altered oxidation and altered nutrition, whilst albumen, epithelium, fibrinous casts, and blood-globules are thrown out in the urine. The substances or their parents that the cortical structure should secrete are left behind in the blood, and from it they pass with the lymph into the structures according to their power of diffusion. In the cellular tissue these lymph effusions can most easily accumulate, and the chemical action set up by the urinous substances acting on the cellular substance probably is the cause of so large an amount of fluid being poured out. It is probable also that sometimes, from the excessive hardness of the effusion in the legs, that some fibrinous as well as albuminous and urinous matters are poured into the cellular tissue.

Sometimes the inflammation in the tubes may be as slight as in the slightest catarrh, lasting a few days and showing scarcely any symptoms. At other times the intensity of the action may be so great that it can only be compared to the most intense croup.

Many cases arising from cold, scarlet fever, irritants, or pressure will require no treatment at all. As soon as the causes pass away the complaint ceases. In other cases the increased action, the mechanical obstruction, and the tertiary diseases are so intense that no time for any treatment is allowed. Thus, after scarlet fever the patient may in a few hours sink from the violence of the secondary disease. In the vast majority of cases of tubular nephritis the disease lasts for some weeks, and is far more influenced by treatment than any other form of Bright's disease.

Another frequent cause of tubular nephritis is scarlet fever.

It has been said that an internal desquamation in scarlet fever causes tubular nephritis, but in the secondary affections of the eyes, ears, and glands after scarlet fever scaling does not occur. Moreover, the scaling of the skin is only the result of the altered nutrition arising chiefly from the increased circulation which the increased chemical action in the skin produced. If shedding of the epithelium does occur in the tubes of the kidney, alterations in the chemical and mechanical actions in the tubes must have preceded this scaling, and these actions, and not the mechanical scaling, are the cause of the tubular nephritis.

Although the scarlet-fever poison has never been isolated, nor its amount at different times determined, yet, judging from small-pox, you may be pretty sure that it multiplies, and that the action which we see on the skin goes on more or less strongly in every part of the body, so that at the time when the eruption begins to decline the amount of poison oxidized or unoxidized in the skin and textures must be at its highest point. This must be taken up by the lymphatics, and must be thrown out by every excreting surface, more especially by the kidneys, through which the greater part of all extraneous substances pass and undergo further oxidation. Even for a fortnight after the eruption declines the elimination of oxidized poison must continue, and during all this time in the kidneys, the eyes, the ears, or the glands unmodified peroxidation may be set up.

Many other poisonous substances, as cholera poison, turpentine, cantharadin, copaibæ, &c., when taken by the stomach, the lungs, or the skin into the blood, probably even in a few minutes begin to pass off by the kidneys, and may give rise to the same tubular nephritis.

A peroxidation spreading up from the pelvis of the kidney; or increase of pressure on the arterial system consequent on obstruction to the free flow of blood in the renal veins—as, for example, during the last weeks of pregnancy—may be mentioned among other causes of tubular nephritis.

On the Signs and Symptoms of Tubular Nephritis.

In all lung affections or bowel troubles you would expect to learn many things from the more or less careful observation of the expectoration or the evacuations. In diseases of the cortical structure of the kidney, without the most careful microscopical examination of the urine, you will get nothing more than the fact that more or less albumen is shown by chemistry to be present. The interpretation of the meaning of the albumen depends on the general history and circumstances under which it occurs, but still more on the microscopical appearances which the urine presents; and without the microscope no accuracy of diagnosis is possible. Common-sense, or even good guessing, without a microscope may lead you right, and the microscope may only help to lead you wrong; but if you become skilful in its use, and not over-refined in drawing conclusions from a single cell or a particle of fibrin, and if you employ it as one of the means, and not as the only help, to a right diagnosis, you will find that in this tubular nephritis more especially it will serve you well.

Masses of epithelium of the form of the renal tubes, fibrinous exudations in casts of the tubes, exudation cells, mucous cells, blood cells, pus cells, these all may occur, in every variety, according to the varying states of congestion, inflammation, and suppurative deposit or production of fat in different parts of the tubes of the kidney at the same or at different times. It is in tubular nephritis that these appearances mostly occur in the urine; and according to the intensity or stage of the attack the microscopic appearances will be more or less pronounced. Moreover, as tubular inflammation is more curable than either of the other forms of cortical disease, so the appearance of these products of inflammation—altered epithelium cells and casts—indicates that the least dangerous of the three diseases is present, and that if the interstitial and vascular structures remain free perfect recovery may take place. Hence excess of fibrinous casts in the urine, other things being favourable, should lead you to a far more hopeful prognosis than when no casts and no tubular epithelium

are found. When cirrhosis or amyloid disease (even in extreme cases) are present, no microscopic appearances may be found; even after careful watching for months for the slightest microscopical evidence of disease, I have found, after death, that the cortical structure of both kidneys had almost entirely disappeared.

Consequences of Tubular Nephritis.

Not only do albumen, fibrin, and blood-globules come out, but urea and its progenitors are prevented from escaping in the urine by the altered conditions produced in the tubes. These urinous substances cannot be kept in the blood, but they diffuse back into every texture, and in the cellular tissue set up increased chemical action, and water, albumen, and sometimes even fibrin are poured out. In the loose cellular tissue under the eyelids the effects of the irritating fluid are generally most perceptible, even when the lowest part of the denser cellular tissue about the ankles shows as yet no appearance of effusion. The more rapidly this acute dropsy comes on, the harder the swelling is to the touch; in other words, the more fibrin is mixed with the other products of this effusion; and in the most intense cases of tubular nephritis, scarcely any impression can be made by the finger even where pressure can be most strongly applied.

This primary urinous acute dropsy differs altogether from the secondary anæmic dropsy, which, in tubular nephritis, and in other forms of Bright's disease, comes on when the blood-globules and albumen in the blood have, by long-continued wrong chemical and mechanical actions, fallen so low as to produce anæmia. Then, as in anæmia from other causes, if little urine is passed, œdema becomes evident in the lowest parts of the limbs or body, and the slightest pressure leaves its mark, and the water can be moved from place to place, because no fibrinous matter has been effused.

The primary dropsy may continue even after the secondary dropsy is set up, for the two causes may be in action at the same time, or the secondary dropsy may more or less quickly come on after the first dropsy has passed away.

When urea and its progenitors exist in the blood, not only does it diffuse into the cellular tissue, but it passes also into the serous and other textures of the different organs. Hence the disposition to pleurisy, pericarditis, peritonitis, pneumonia, bronchitis, and other secondary diseases, which so readily occur in acute tubular nephritis. Even the affection of the brain which occasionally is met with in the most acute tubular nephritis must be attributed to a strong chemical action on the nervous substance, rather than to the slower poisonous action of the urinous matters which I have brought before you when speaking of uræmia. Increased oxidation, in the form of a more or less acute inflammation, may be set up in one or all of the different textures of which the different organs are composed; whilst in uræmic poisoning probably increase of oxidation more rarely takes place.

The Treatment of Tubular Nephritis.

The first indication is, as far as possible, to remove the causes of the attack. When cold is the cause, warm baths, vapour baths, and warm clothing may help to restore the action of the skin. Tartarised antimony has no strong action on the kidneys, and has a very decided action on the skin; and when it acts on the bowels or on the stomach, causing vomiting, it removes urinous substances from the blood. Hence it is a most important remedy in the acute dropsy from cold. Even when poisonous substances are passing out of the blood, as after scarlet fever, cantharides, turpentine, in extreme cases tartarised antimony may sometimes be used. In slight cases simple dilution with the purest water washes the impurity out of the blood.

The second indication is to stop the thickening of the tubes and to relieve the obstructed vessels. Abstraction of blood by cupping-glasses on the loins can hardly be expected to affect the circulation in the tubes of the cortical structure of the kidney; whilst general bleeding, even to a few ounces, has a distinct effect on the pressure of the blood in the malpighian tufts. Hence, if blood at all is taken, it should be by venesection. Digitaline in small doses acts on the nerves

that regulate the circulation like a stimulant, but in large doses or long continued it diminishes the pressure on the arteries; and of all diuretics this is the only one which is admissible in acute tubular nephritis. As the disease becomes more chronic iodide of potassium may be used in diuretic doses. In ten minutes after the first dose it is present in every part of the kidney, and probably may be found there for many days after the last dose has been taken.

The last indication is to relieve the symptoms and complications that occur.

Of these, the dropsy is the most important. In the acute stage you have to contend with the urinous dropsy. For this vapour baths or hot-air baths, used to the greatest extent that the strength will bear, are very efficacious. Then try strong action on the bowels by those watery cathartics that have the least action on the kidneys—as, for example, jalap, gamboge, and elaterium. If the strength admits of it, emetics, tartarised antimony, and ipecacuan may be given.

When the acute stage is over, the tendency to anæmic dropsy begins. To prevent this iron in small doses is the best remedy. Nitre, cream of tartar, broom tea, and other diuretics may be used at the same time, occasionally in very large doses. Even tincture of cantharides may, in the more chronic state, be prescribed. In a very short time the whole of the anæmic dropsy may be thus removed, and then iron, in larger quantity, should be given to prevent a return of the effusion.

The treatment of the secondary inflammations should be carried on with allowance for the general debility which will appear when the increased arterial action subsides.

Counter-irritation is to be preferred to local bleeding, because it saves the red blood. Mercury is hardly ever to be used, as in all forms of Bright's disease its poisonous action is most quickly and violently set up.

LECTURE XII.

ON FERMENTATIONS AND FEVERS.

There is for the chemist and for the physician no subject more anxiously waiting for perfect solution than the nature of fermentation. For animal poisonings are fermentations, including as I intend to do under this term catalytic as well as transferred actions.

Many mineral, vegetable, and animal substances have the power to exalt or change the chemical actions going on in contact with them. Thus heated spongy platinum will cause hydrogen and oxygen to combine. Phosphorus will convert oxygen into the more active ozone. Finely-divided platinum will oxidize alcohol in the air. Peculiar vegetable mycoderms will produce the same oxidizing action as the spongy platinum.

Sugar, when fully oxidized, without the presence of any modifying substance, gives rise to carbonic acid and water only; when modifying substances are present the oxidation is far more complex. With yeast or wine-ferment sugar gives alcohol, glycerine, succinic acid, and carbonic acid; with a different ferment lactic acid is formed; with yet another viscous fermentation occurs, and gum, mannite, water, and carbonic acid are produced. According to M. Pasteur, when animal matters are present with the sugar, oxidation at first occurs; infusoria, as monas crepusculum and bacterium termo, live until the oxygen is gone; then butyric vibrios appear, and these set up putrefaction, and the compound sugar, $ЄH_{12}Θ_6$, gives rise to butyric acid, $Є_4H_8Θ_2$, carbonic acid, $Є_2Θ_4$, and free hydrogen, H_4.

In the human body many different kinds of ferments occur in health. Of these zymases, four are well known: first, that which changes starch into sugar, as in saliva, in pancreatic fluid, in intestinal fluid, and in the liver; secondly,

that which changes sugar into lactic acid, as in the stomach, and in milk; thirdly, that which helps to make the albuminous part of the food soluble, as in the pepsine of the stomach; fourthly, substances that cause the fine division or emulsion of fat in the body, as in bile, in pancreatic and intestinal fluid.

Moreover, many other chemical actions in the human body depend in health on some kind of contact action, or action by presence. The whole process of assimilation in each part of the body—the food becoming blood, the blood becoming part of each organ and texture, identical in composition with the substance already there, gives evidence of the highest amount of contact action, on which clear ideas are as yet wanting.

At present our knowledge of the chemistry of fermentation is insufficient for the full solution of the comparatively simple problems of the making of bread or the putrefying of urine; how far short, then, must it be from giving us the explanation of the chemistry of assimilation?—far less can it help us now to comprehend the great problem of reproduction.

I am unable here to enter into the multitude of questions connected with fermentation in general. I am obliged to limit myself to a few points connected with fermentation, and I shall take that of the urine, on which I have some facts which I wish to bring before you.

First; on acid fermentation in the urine.

For the last twenty years it has been a received opinion that there is an acid fermentation in the urine.* Scherer thinks that after it has been passed an increase of acidity may be observed, and the deposit of uric acid and of acid urates he holds to be well explained by this after-formation of acid. When making my experiments on the variations of the acidity of the urine by carefully determining the amount of acid in the urine at different periods after the water was passed, I was led to doubt the existence of this acid fermentation, and to satisfy myself I made the following experiments on the so-called acid fermentation.

* 'Scherer Beitrage zur Pathologischen Chemie: Annalen der Chemie und Pharmacie,' vol. xlii., p. 176.

I endeavoured to measure the increase of acidity in the urine, first by a standard solution of soda, and secondly, by watching the time when the uric acid crystallized out. A very dilute standard solution of soda was prepared, and eighteen different experiments on healthy urine were made. The acidity was determined when the urine was first made in a fixed quantity of water, 50 or 100 c.c., and the acidity was again and again noted from time to time on different days in the same urine. The results are given in the following table:—

	Expt. 1st.	Expt. 2nd.	Expt. 3rd.	Expt. 4th.	Expt. 5th.	Expt. 6th.	Expt. 7th.	Expt. 8th.	Expt. 9th.
1st day .	..	..	..	..	..	..	..	..	..
2nd day .	..	no incr.	no incr.	no incr.	slight incr.	..	..	..	..
3rd day .	no incr.	..	..	..	..	slight incr.	slight incr.	decr.	incr.
4th day .	..	..	..	no incr.	no incr.	..	..	..	..
5th day .	no incr.	no incr.	..	..	..	slight incr.	slight incr.	slight incr.	..
6th day .	..	..	..	no incr.	..	..	..	..	decr.
7th day .	no incr.	no incr.	..	..	no incr.	slight decr.	..	decr.	..
8th day .	..	..	..	..	..	..	..	..	..
9th day .	..	..	..	..	..	slight incr.	..	same	..
10th day .	decr.	..	..	..	decr.	..	..	..	..

	Expt. 10th.	Expt. 11th.	Expt. 12th.	Expt. 13th.	Expt. 14th.	Expt. 15th.	Expt. 16th.	Expt. 17th.	Expt. 18th.
1st day .	..	..	..	..	..	..	..	no incr.	..
2nd day .	no incr.	slight incr.	..	..	..	no incr.	slight incr.	..	slight incr.
3rd day .	..	..	..	..	..	..	..	no incr.	..
4th day .	no incr.	slight incr.	..	..	..	..	..	..	..
5th day .	..	..	slight decr.	strong decr.	..	..	..	..	..
6th day .	decr.	slight incr.	..	..	no incr.	..	..	no incr.	..
7th day .	..	..	..	..	..	..	..	..	..
8th day .	decr.	..	..	..	..	..	..	decr.	..
9th day .	..	..	..	..	..	..	..	..	..
10th day .	..	..	..	..	..	..	..	..	..

Thus, in all these experiments there is not one that showed any decided increase of acidity. There was either no increase of acidity at all, or it was so slight that the increase was not beyond the possible error of observation consequent on the process. Failing by direct measurement, I tried whether any conclusion could be arrived at by noting the time when free uric acid crystallized out, because the crystallizing out of free uric acid is the most delicate test of the free acidity of the urine. Forty-nine different urines were observed daily without any filtration to determine the day when the uric acid crystallized out. In 32 no crystals were found; in 17 they were found.

In these 17	urines	crystals	were seen	5	times on	the 2nd	day.
,,	,,	,,	,,	5	,,	3rd	,,
,,	,,	,,	,,	2	,,	5th	,,
,,	,,	,,	,,	1	,,	6th	,,
,,	,,	,,	,,	2	,,	7th	,,
,,	,,	,,	,,	1	,,	11th	,,
,,	,,	,,	,,	1	,,	12th	,,

Twenty different urines were filtered immediately after they were passed, and in these only ten times were crystals of uric acid found.

In these 10	urines	crystals	were seen	3	times on	the 3rd	day.
,,	,,	,,	,,	3	,,	4th	,,
,,	,,	,,	,,	3	,,	5th	,,
,,	,,	,,	,,	1	,,	7th	,,

It follows, then, that there is no evidence of any increase of acidity at any fixed short period after the urine is made. No proof of fermentation can be drawn from these observations of the days of appearance of uric-acid crystals in the urine.

When Professor Brücke observed that in health small quantities of sugar were found in the urine, it seemed to me very desirable to try whether this sugar disappeared when the urine was kept. Three litres of urine were divided into two perfectly equal portions. One part had the sugar determined immediately; it gave 2·4 grains of sugar. The other part was kept until it became feebly alkaline in twenty-five days.

Then the sugar present in it was determined by the same process, and found to be 1·9 grains.

Hence I can find no distinct evidence of an acid fermentation in the urine. The more or less rapid crystallization of free uric acid depends on the amount of liberating acid that is secreted by the kidney and on the more or less acid urates that exist in the urine, and on the influence of other salts present at the same time. Highly-acid urates are decomposed, setting free uric acid, when washed with water or salt and water alone; while they are not decomposed if washed with the urine from which they were precipitated. Less acid urates liberate uric acid when washed with dilute solutions of acid or of pure acid phosphate of soda more or less quickly, according to the amount of dilute acid or acid phosphate of soda present, and according to the temperature and the time the action is continued. Even in the ordinary method of determining with strong hydrochloric acid the amount of uric acid in the urine, twenty-four hours are, as Dr. Hassall has shown, insufficient to allow all the uric acid to crystallize out.

Secondly, on the alkaline fermentation in the urine.

It has been said, and repeated over and over again, that the mucus in the urine is the ferment that effects this change from acid to alkali; but this is not the fact, as the following experiments, not made for this object, will show you.

In November the fresh urine was filtered carefully through a fine filter, and twenty observations were made from day to day. Seven times the urine became neutral or alkaline on the following days:—Ninth day, 1; tenth day, 2; eleventh day, 3; sixteenth day, 1.

In February the unfiltered urine was observed twenty-two times. Nine times it became neutral or alkaline on the following days:—Fifth day, 1; sixth day, 1; eighth day, 1; ninth day, 2; tenth day, 1; eleventh day, 1; thirteenth day, 1; fourteenth day, 1.

In June the unfiltered urine was observed twenty-seven times. Eighteen times it became neutral or alkaline on the following days:—Fourth day, 1; fifth day, 1; sixth day, 2; seventh day, 3; eighth day, 4; tenth day, 2; eleventh day, 5.

Hence, filtered, 7 in 20 become neutral or alkaline during observation, most on the eleventh day; unfiltered, 9 in 22, most on the ninth day; in summer, unfiltered, 18 in 27, most on the eleventh day. So that there is no decided difference between filtered and unfiltered urine as regards alkaline fermentation. The mucus that is separable by the filter is not the ferment that changes the urea into ammonium carbonate, $ϴH_4N_2ϴ + H_4ϴ_2 = 2(NH_4)ϴϴ_3$.

Moreover, vibrios are not the cause of the alkalescence; for I have several times met with urine that was exceedingly foul in smell at the moment of passing, and so ropy that the drops adhered as they were poured from the vessel, quite distinctly tailing. Yet test-paper showed that this water was highly acid, and it remained so in one case in July for seven days. With the microscope, multitudes of active vibrios were found within a few minutes of the water leaving the bladder.

That these vibrios are formed within the bladder the following case proves :—

A boy, eight years of age, was brought to me with the following history :—A native of India, just arrived, sickly, thin, sallow, languid. When four and a-half some unusual smell was first perceived in the urine; but little was thought of it until he embarked for England, when the water was observed to be passed in large quantities, and frequently to be so abominably offensive as to render his cabin intolerable to those with him. The mother remarked that she had observed the offensive smell to be always most perceptible when the bowels were most constipated. When the bowels were well evacuated the urine was not fœtid. Generally fifty to sixty-five ounces were passed in twenty-four hours. At one evacuation of the bladder he did pass thirty-three ounces; specific gravity 1008; slightly acid; with albumen and pus, and no casts of tubes. Specific gravity sometimes as low as 1004. Dr. Prout, who examined the patient, considered the smell was distinctly that of sulphuretted hydrogen. Two months after I saw him he caught a bad cold in Ireland and died. The kidneys and bladder were sent to London for ex-

amination. The right kidney was one and a-quarter inch long, one inch broad, and the ureter impervious. The left kidney was large, with abscesses in it. The pelvis and the ureter were dilated. The bladder was very much dilated. The right impervious ureter opened by wide mouth into the bladder. At its entrance it admitted a large catheter, and it swelled, when blown up, to four times the size it had when collapsed, presenting very much the appearance of an inflated small intestine. It was twice the size of the other ureter, and was four inches long. During life the urine was caught on a glass at the microscope, and the focus being right the infusoria were seen instantly in activity in four seconds. As many as fourteen divisions were counted in one moving string; monads were also present, and some pus-globules and blood-globules.

M. Pasteur considers that he has proved that the germs of these vibrios come from the atmosphere, and that they will not form unless all the oxygen present is first taken away by other kinds of infusoria; then the vibrios set up intense putrefaction, and without the access of germs and absence of oxygen no putrefaction occurs. When air is present, he says, in twenty-four hours monads and bacteria abstract oxygen, and grow on the surface in contact with the air, forming a pellicle, which gets thicker and thicker until it falls to the bottom, and thus prevents oxygen getting to the lowest part of the liquid. There the vibrios can live and do set up putrefaction, transforming nitrogenized into simpler, but still complex compounds. Bacteria burn these products, and reduce them to the simplest forms—water, ammonia, and carbonic acid.

The alkaline fermentation of the urine and putrefaction in the bladder are not explained by these facts of M. Pasteur. If it be possible that monads or vibrios do make the urea change to ammonium carbonate, then the germs of the monads and of the vibrios, at least sometimes, must be formed in the bladder. The putrid abscesses found in the liver, and those in contact with bone, or in the cellular tissue and in other parts where no germs can be carried by the access of air, must either prove that vibrios are not necessary to putrefaction

or that the germs of infusoria must during life pass into all our textures and start into activity when circumstances permit. At present, notwithstanding M. Pasteur's high authority, the possibility of the production of infusoria without germs entering the body must be considered an open question.

If we are not able yet to comprehend the alkaline fermentation of the urine and the putrefactions that occur in the bladder,* how can we now expect to obtain an explanation of other more complex fermentations that may arise within the body? For example:—

M. Davine has shown that the Charbon contageux, or sang du rate or malignant pustule depends on the development of bacteria in the blood; if the disease is local, it gives rise to carbuncle, or diffuse erysipelas; or if general, it affects the whole blood. The infusoria are analogous to those which produce butyric fermentation. Fourteen inoculations on rabbits proved that the blood was affected. In four hours the rabbits died. The blood was decomposed and full of infusoria. The organs, as, for example, the liver, &c., were decomposing, and ecchymosis and effusions were found in the serous cavities. In man the disease has been attributed to inoculation by bites from flies fed on putrid matter.

* Since this was written, M. Béchamp, in the 'Comptes Rendus' for 27th February and 7th August, 1865, stated that he has insulated by alcohol the ferment from the urine. He names it Néfrozymase, and he traces its variations in healthy and diseased states. It is a soluble organic albuminous substance, void of all organization, able, though to a much less degree, than sialozymase or diastase, to change starch into dextrin and sugar. It is altered by boiling, and then loses the property of acting on starch or on urea. This may be shown to be the case even in healthy urine, without any separation of the néfrozymase. Thus M. Béchamp brings us back again to chemical changes taking place in a peculiar albumen as the cause of the decomposition of urea in the urine, whilst M. Pasteur holds that living vibrios effect this change. Between a highly-complex organic substance undergoing chemical change, and the chemical actions going on in living plants and animals, lies our future knowledge of fermentation and putrefaction. Most probably it will ultimately be proved that when in living or in dead animal or vegetable albuminous matter certain kinds of increased chemical action are set up, the various kinds of fermentation or putrefaction are produced, according to the kind of chemical action that exists in the so-called living or dead albumen.

Consequences of Ammoniacal Urine.

The effect of this change of urea into carbonate of ammonia in the urine has been the cause of great confusion. It was exalted into a disease, and the chemical inability of carbonate of ammonia to dissolve earthy phosphates in the urine was called the phosphatic diathesis; and to make the confusion still worse, as the amount of earthy phosphate precipitable depends on the amount of earths present, when much magnesia and lime were in the ammoniacal urine the phosphatic diathesis was considered very marked, and very slight when a small amount of earthy matter was present. Carbonate of ammonia and earthy salts in the urine give rise to all the appearances that have been attributed to this disease, and the cause of the phosphatic diathesis disappears in the cause of ammoniacal urine—in other words, it depends only on the alkaline fermentation which we have just been considering.

The Symptoms Resulting from Ammoniacal Urine.

The bladder in health contains a feebly acid saline fluid. If the acid or salts vary greatly on either side of the usual amount the bladder is irritated by the unaccustomed stimulus of pure water or excess of salt. Thus a very strong solution of salts in the urine, or very dilute, almost watery urine, cause irritation. Highly acid urine and, above all, ammoniacal urine have the same effect. Increased irritation causes increased secretion, and the mucus cells when thrown out in quantity, acted on by the carbonate of ammonia, become ropy and adhesive, like the ordinary alkaline mucus from other mucous membranes, as from the nostrils. If the irritation is continued pus is formed, and these cells also when acted on by carbonate of ammonia become ropy, and this has also been included under the term of ropy mucus. According as more or less earthy phosphates are present—that is, according as more or less magnesia or lime is taken into the system, more or less phosphatic precipitate is mixed with the ropy mucus or ropy pus, and this chemical error mounts up to the formation of

mechanical masses of mortar-like or stony substances, which cause extensive pain either in passing through the irritated urethra or in scraping the inflamed surface of the bladder, or even by precipitation within the mucous membrane of the bladder itself.

The constant muscular contraction to expel the irritant is more disturbing to sleep than the cough of bronchitis; and hence loss of rest becomes sometimes the most serious consequence of the complaint. Next to this is the extension of the inflammation upwards to the pelvis of the kidney. The ureters may show or not show that they have been inflamed; sometimes no trace can be found of the passage of the inflammation upwards, but pyelitis and tubular nephritis, producing pus throughout the kidneys and uræmia throughout the body, may put an end to the progress of the disease by destroying life.

The inflammation may spread downwards, and then the urethra suffers, and often violent orchitis is set up.

If the neck of the bladder and the prostate get thickened by interstitial deposit of fibrin, the bladder is unable to empty itself, and the fluid that remains is in a variable state of more or less complete putrefaction. If the fundus is chiefly thickened by deposit and increase of the muscular coat it will contain less and less fluid as the thickening increases; from either cause the frequency of the calls also increases, and when ulceration takes place the amount of pain with each contraction becomes excessive.

Treatment of Ammoniacal Urine.

The treatment of ammoniacal urine resolves itself into keeping the urine acid and stopping the inflammatory action; and as the alkalescence by its chemical action keeps up the inflammation, the stoppage of the formation of carbonate of ammonia in the bladder becomes the main object to be attained.

Usually, as the urine comes into the bladder, it is acid; as soon as it gets there it finds some ammoniacal urine there

already; this not only neutralises the acid that comes from the kidney, but sets up decomposition of the urea, and forms fresh carbonate of ammonia; so that the removal of the ammoniacal urine that remains in the bladder is absolutely necessary, unless sufficient acid can be made to come from the kidney to neutralise it.

Vegetable acids far more quickly run off in the urine than mineral acids, of which sufficient cannot be taken to pass in quantity through the kidneys. Of all the acids lemon-juice is perhaps the best which can be used. Many years since Mr. Witt made the following analysis of lemon-juice for me (see 'Quarterly Journal of Chemical Society,' vol. vii., p. 44):—One ounce (480 grs.) of lemon-juice contains only 1·728 gr. of inorganic constituents; of which, potash, sulphuric and carbonic acids constitute three-fourths; phosphoric acid, soda, and lime, with traces of silica, and iron and magnesia, constitute the other fourth. Hence water and citric acid constitute by far the largest part of the lemon-juice, the citric acid being, on an average, about 40 grs. to the ounce of juice.

It is highly probable that citric acid and other vegetable acids have an anti-inflammatory action (lessening the oxidation that exists) wherever they are carried, and they not only pass to the kidneys, but probably diffuse into every part of the mucous membrane of the bladder; to a small degree lessening the alkalescence of the textures in which the peroxidation is going on.

The citric acid must not be taken in such quantity that it irritates the stomach and bowels, nor should it set free uric acid in the urine. So that the highest limit can be easily recognised by the bowel symptoms. The lowest limit is so much as will just make the urine acid. This cannot always be reached. Three, four, five, ten lemons or more daily will sometimes not neutralise the alkali in the urine, but may so stop oxidation and nutrition that the body may become feeble and wasted. Before this effect is produced some other way of removing the ammonia must be tried. Taking away the alkaline urine by the catheter so frequently that a smaller

quantity of lemon-juice will keep the water acid is easy when the passage of the catheter does not cause mechanical irritation to take the place of the chemical irritant. The catheter must be used more or less frequently, according to the reaction of the urine. If drawing off the water at night whilst taking lemon-juice or other acid keeps the urine feebly acid, no further mechanical means are required; if not, then, twice, thrice, four times daily the water must be drawn off; and even, in extreme cases, the catheter must be kept in the bladder, so as to free the urine continually without the irritation of the passage of the instrument; but the presence of the foreign body in the bladder, even when perfect rest is observed, often causes so much irritation that it becomes an aggravation of the disease. Moreover, by washing the bladder with small quantities of hydrochloric or acetic acid and water, after the urine is drawn off with the catheter, the ammonia may be easily neutralised, and a very small quantity of feebly-acid fluid may be left in the bladder to counteract the decomposition of the urea, and to make the surface of the bladder itself less foul. How frequently the washing should be repeated, and what the strength of the acid injected should be, ought to be determined by the reaction of test-paper or the smell of the urine. Whatever you do, remember that the object is to get rid of a chemical irritant, and that if by rough handling of the catheter, by its too frequent use, or by too strong an injection you mechanically or chemically irritate the bladder more than it is irritated chemically by the ammoniacal urine, no good will come from your treatment.

When you have removed or can prevent the ammonia of the urine, then balsamic remedies, as in bronchitis, are often useful. These pass from the kidneys and also directly from the blood to the mucous membrane. Buchu, cubebs, copaibæ, turpentine, eau de goudron (purified tar water), all these may be useful; remembering here, also, that if the stimulant be too great, harm may be done by setting up fresh action. Astringents, as any preparation of gallic acid, tannic acid, uva ursi, rhatany, catechu, matico, alum, lessen the secre-

tion of pus and mucus by their action upon the mucous membrane.

Tonics also often are useful when the acute symptoms subside—among these are quinine, biberine, pereira brava, and other bitters.

On Fevers; or Qualitative and Quantitative Errors of Peroxidation.

The term zymotic disease, which implies a chemical action, is now, thanks to Dr. Farr, in ordinary use. This term means that different vegetable or animal ferments, living or dead, albuminoid substances in certain states of chemical change, can be formed within or can pass from without into the body, and, taking part in the actions going on there, can produce different diseases. Generally speaking, fermentation may be considered as a peculiar oxidation in which carbonic acid and water and heat are produced; but instead of a dual action of oxygen on organic substance, fermentation consists in the mutual action of three substançes—namely, oxygen, the organic matter, and the ferment. These three substances interfere not only in the chemical actions of oxygen, but also in those of nutrition; so that a long list of substances might be formed, beginning with the spermatozoon and passing through torulæ, until we come to pepsine, which are capable in health or in disease of so increasing or altering the chemical actions of oxidation and nutrition in the body that quantitative or qualitative results are obtained which would not have been reached by the ordinary actions without the intervention of the third substance.

It will only be possible for me in this lecture shortly to bring before you one or two of these diseases of fermentation; and on account of the intensity of the chemical action which occurs I shall class them together as diseases of modified peroxidation. Among these I place small-pox, scarlet fever, measles, typhus fever, as the most striking examples; typhoid fever, yellow fever, ague, are lower in the same class; whilst syphilis and cancer are highest in the class in which there is

modified chemistry of nutrition, but no distinct evidence as yet of increased oxidation.

Of all the modified peroxidations that can occur in the body, small-pox is the most definite, because the poison can be got apart, and the quantity necessary for producing the action can be fixed, and through the most glorious discovery of vaccination it can be set in action whenever we please. We can almost see it passing from the cellular tissue into the blood, and from the blood into every particle of every texture, rendering it incapable of undergoing the same action again.

Let us look a little closer at this action of small-pox poison. If the minutest particle of substance, a little dried albuminoid substance, in a peculiar chemical state of action, on a lancet, or in the dust of the air, is put into the cellular tissue or is inhaled into the lungs, it passes on to the blood, and through it into every texture. In a few days the chemical actions of oxidation and nutrition throughout the body are altered, and the particle of matter has reproduced itself immeasurably. The violently increased chemical action, the peroxidation, is shown by the increased heat of the body, the violent fever. The altered nutrition is evident not only in the eruption of pustules in the cellular tissue under the skin, but in the altered condition of the blood and in all the textures of the body; each particle of substance being rendered incapable of undergoing the same process again, and by assimilation every future particle that takes the place of every modified particle is also generally incapable of being modified again.

Throughout the course of the general peroxidation, and more especially at the end of the fermentation, local peroxidations frequently come on in any part of the body. Inflammations of the eyes, the ears, the mucous membranes, the joints, the serous membranes, the parenchymatous tissues, anywhere an unmodified peroxidation is ready to begin, and this easily gives rise to suppuration or causes obstructions which the feeble circulation cannot overcome.

The most striking facts concerning this small-pox ferment are, first, the very small quantity of substance that produces so much effect; secondly, the immeasurable increase of the

poison in the body, each pustule having the same property as the original ferment; thirdly, the period of incubation during which the poison must at first slowly increase in every texture, and there give rise to the modified peroxidation and altered nutrition which constitute the attack.

The poisons of scarlet fever, of measles, and of typhus, though less tangible, are not less substantial than the small-pox ferment. Like it they can most probably be dried and carried from place to place and pass into the mouth with the dust which we each moment inhale or swallow. In chemical composition scarlet fever, measles, and typhus ferments most probably resemble albumen in complexity, and, like albumen, they may be altered in composition and action by heat, alcohol, arsenic, tar acids, and many metallic salts. As soon as they reach any spot where they can oxidise, they set up an oxidation and reproduction in each contiguous particle of albuminous substance. From the cellular tissue, the air-passages, or the stomach or bowels, the contact action spreads into the blood, and there it multiplies, whilst it is carried into all the capillaries, and through them into every texture of the body; then the increased oxidation and formation of ferment becomes most violent, and fever to a greater or less degree is present. Long after the strongest action is reached, a slower action continues, and at any time or in any part or texture of the body, whilst the specific chemistry is going on, an ordinary local peroxidation may be lit up, and a more or less acute inflammation may be added to or follow the fever which the ferment had produced.

During the height of the fermentation in typhus fever, the heat may rise to 5, 6, or even 10° Fah. above the ordinary temperature; and when the fermentation is ended, the albuminous textures of the body are so changed that they are incapable of going through the same process again. Between these two results there are innumerable other products of chemical change, varying with the kind and degree of fermentation. In typhus fever it is said that urea is increased and carbonic acid diminished. To these and a multitude of other chemical questions regarding fermentation chemistry

will give definite answers; but above all questions, one of the most difficult to answer and yet one of the most important, is the amount of oxygen that is consumed in the different kinds and degrees of peroxidation which can take place within us.

In each organ, according to the intensity of the action set up by the ferment, altered functions may arise, and these may be still more altered when an ordinary peroxidation at the same time takes place. Thus the brain, heart, lungs, kidneys, liver, or any texture composing these organs may show by more or less wrong mechanical results the effect of the ordinary modified peroxidation; and the effects of the fever and of the inflammation may be so mixed that neither during life nor after death may any accurate separation be possible.

Closely related in chemical composition to these violent ferments are the less active ferments of ague and typhoid fever. There is so little difference in the chemical composition of animal and vegetable substances, that the distinction between animal and vegetable poisons is no longer possible. Vegetable albuminous matter undergoing change may produce almost, if not quite, exactly the same poison as animal albuminous matter. Hence, probably, the resemblance between ague poison and typhoid fever poison, and the possibility that sometimes one and sometimes the other of these poisons may be formed from the same changing matter under different circumstances.

Ague ferment is probably a highly-complex nitrogenous substance, capable of being dried and carried by the wind far from the place where it was produced. It enters by the mouth with the dust, and, like animal or vegetable alkaloids, it passes from the blood into every texture of the body, and acts on each much or little according to its chemical properties. Perhaps it acts first most strongly on the nerves that regulate circulation, causing for a time contraction of the arterial vessels and consequent suboxidation everywhere. But this soon passes into a state of peroxidation, partly from the obstruction of the small arteries increasing the pressure of the heart, and partly from the changes going on in the textures and in the poison by which it is partially destroyed. During the remis-

sion, probably the poison is reproduced until sufficient, in from one day to three days is formed to go through the same actions again.

This theory of ague admits of a reasonable explanation of the action of quinine and arsenic in stopping the paroxysms of the complaint. On the ague poison itself quinine and arsenic may have no action, but they pass into every texture from the blood, and, combining with the nervous and other substances on which the ague poison acts, they form compounds on which the ague poison is incapable of producing an effect before it is oxidised and destroyed.

The ague poison, unlike the small-pox or typhus fever ferment, instead of protecting the body by making it incapable of undergoing the same action again, makes the nerves more ready on the slightest renewal of the poison to set up the same train of phenomena again; so that it has been said that the ague poison may lie dormant for years. It is far more probable that a much smaller quantity of the poison can produce the return of the symptoms than that the original ferment should retain its properties for months, or even for years, after its first action had passed by. In this respect, and in some others, the action of ague poison proves that it is a very peculiar ferment, and hence, though I have placed it near to the typhoid ferment because of its origin, I must shortly point out to you the different effect which the true typhoid ferment produces.

The typhoid ferment is probably formed out of vegetable or animal albuminous substance. In sewers, in drains, in ditches, possibly even in the drains of the human body, a substance may be formed which is not volatile in itself, but by foul gases or currents of air can be carried into the mouth, and in some period between a few hours and fourteen days it sets up a modified peroxidation. More slowly absorbed and less rapidly reproduced and changed than typhus ferment, it passes into the blood, and from it into each texture; whilst some of the poison has a local action on the glands of the small intestine, and produces increased action, effusion, obstruction, and retrograde action, causing ulceration, sloughing, and even perfora-

tion, by which mechanically the contents of the bowel may escape and an uncontrollable simple peroxidation may be set up. The poison that has passed into the tissues acts on each organ more slowly than the typhus poison ; still, like it, everywhere it gives rise to altered functions, and everywhere local peroxidations are ready to occur ; bronchitis, pneumonia, peritonitis, tubular nephritis, cystitis—any of these and many other inflammations may be set up at any time during the course of the fever. Probably the substances produced by the increased chemical action in typhus and typhoid fever will be found to be very similar. There may be the same amount of heat, the same excess of urea, the same excess of antecedent substances from which the urea is formed ; possibly the same consumption of oxygen when the same temperature in each fever occurs ; but in the properties of the ferment formed in the body a distinct difference of diffusibility must exist, the typhus poison passing with greater ease into neighbouring bodies ; whilst the typhoid poison rarely, if ever, is communicated by infection.

On the Mechanical Disorders that arise out of the Chemical Errors in Fevers.

In all fevers and inflammations any increase of chemical action in the textures immediately produces an increase of circulation and of mechanical pressure in the capillaries. This may so increase as to cause obstruction of the blood-vessels. Increased pressure of the heart is then produced, and this may remove the obstacle or may add to the congestion. As the mechanical obstruction increases all the chemical changes lessen, and finally may be entirely stopped, and thus even local death may take place.

In all fevers also the loss of mechanical power is quite as remarkable as the increase of chemical action. The chief amount of energy liberated by the action of oxygen in the body seems expended in the production of heat, so that far less than the ordinary amount of power remains to be employed in the production of mechanical motion. The muscles

may be considered as machines made for the conversion of chemical force into mechanical motion. How this is done cannot be explained in the present state of our knowledge of the mechanical, chemical, or electrical actions in the muscle; but that the muscular force arises from some equivalent force, and sooner or later must come from the chemical force in oxygen, hydrogen, and carbon, opens an immense field for investigation, and is easier of belief than that force should be each moment created and destroyed. The amount of sugar and fat present in any muscle would perhaps be used up if in the working of the muscle itself fresh fuel was not produced. The action of oxygen on the syntonin in the muscle may be direct, and may give rise to the force required; but it is more probable that the syntonin splits into substances of two classes, one ending in urea, which is incapable almost of combustion, the other in inosit, which would immediately give water and carbonic acid.

In fever the poisonous ferment in the muscle probably determines a different chemical action from that which takes place in the muscle in health. The increased heat and increased urea mark the increased action, but loss of motor-power in the muscles shows that the conversion of chemical into mechanical force does not take place.

This mechanical disorder becomes by its action on the muscles of respiration or circulation the source of complications and dangers in fever to which I must shortly allude. Gradually in the course of fevers the sounds of the heart may be found to become more and more feeble, and the respiration, without any wrong in the lung, becomes shallow and weak from the diminished power in the muscular tissue. The diminished tension in the arteries has a direct effect upon the circulation through the capillaries, and the motion in the veins is more or less stopped; hence congestion of blood in the venous system occurs, and hæmorrhages, effusions, and coagulations in the veins may take place anywhere. The imperfect action of the muscles of respiration produces the same mechanical effects in the circulation through the lungs; imperfect oxygenation takes place in the lungs from the stoppage of

blood in the pulmonary veins; without any inflammation, œdema of the lungs, hypostatic consolidation may occur. The circulation through the lung is so feeble that even the force of gravity acting on the blood in the lungs cannot be counteracted, and accumulation takes place in the most dependent parts.

The muscles of the bladder are also so weakened that the urine accumulates, and frequently external muscular pressure is required after the catheter has been passed to cause the urine to flow.

In another large class of zymotic diseases the qualitative and quantitative errors of oxidation are scarcely detectable, whilst the qualitative and quantitative errors of nutrition chiefly mark the action of the poison.

Of these diseases true syphilis may be taken as the type.

It can scarcely now be doubted that the actions of two poisons have been included under the term syphilis. The first, like impetigo, is capable of being communicated, and often repeated, because it exists only locally or passes up to the nearest lymphatic glands; whilst in the true syphilis the poison from the local sore enters the blood and passes from it into each texture, where it multiplies and produces changes of nutrition, and partly unchanged, and partly changed in composition, passes out perhaps in each secretion.

This true syphilitic ferment resembles very closely the small-pox ferment in the universal diffusion of the poison, and in the consequent protection it sometimes gives from another attack by rendering a second similar change in each texture impossible. The protective power of the alteration is to a slighter degree extended to the progeny through the germ and spermatozoon; so that a race partly protected by inheritance may suffer less from these diseases than a purer race, whose textures are free to undergo the full change which constitutes the disease. Both poisons give rise to increased cell growths, effusions, oxidations, congestions, and ulcerations; and these may take place in any part of the body, when the poison exists everywhere.

True syphilis differs, however, altogether from small-pox in

its definiteness of course as to time. Syphilis produces no fever to terminate the fermentation in a definite period, and it may consequently remain active or dormant in the textures for years.

It is vain now to ask what circumstances at the end of the fifteenth century produced the first modified albuminoid matter which gave rise to the first true syphilitic poison. In cancer, which bears a distant resemblance to syphilis, although the spontaneous generation of the first cancer cell is daily occurring in some predisposed texture, yet we are as yet quite unable to say what produces the first modified particle of matter which multiplies and communicates its composition to adjacent predisposed textures by contact, and is carried by lymphatics and blood-vessels to every part of the body, and affects the nutrition of each part with which it comes in contact, provided the textures are in a condition to propagate the cancer cells.

Another instance of spontaneous generation of a poisonous ferment is presented to us in rabies; and with this poison also, unless a peculiar condition of system exists, the ferment when inserted has no action; and here also our knowledge is at present unable to say what circumstances determine the formation of the first particle of poisonous saliva; except by its effects, the peculiar change in the albuminoid matter of the saliva in the present state of chemical knowledge could not be recognised.

PART IV.

ON GENERAL AND LOCAL CHEMICAL AND MECHANICAL DISORDERS ARISING FROM ERRORS OF CHEMISTRY IN THE DEVELOPMENT AND REPAIR OF THE BODY.

LECTURE XIII.

ON SUBTROPHIC AND PERTROPHIC ACTIONS.

Instead of giving you one lecture on this subject it might well, from its vastness, furnish me with materials for a complete course, for the chemistry of nutrition is much more complex than the chemistry of oxidation because it includes not only the chemistry of the formation of the tissues or the assimilation of the albuminous principles of the blood to each organ, but also the chemistry of the removal of the used materials. This chemical building up and chemical taking down must have a direct dependence the one on the other, both in the substances taking part in the quality of the actions, and in the rate at which those actions are carried on.

Moreover, oxidation is actively concerned in rendering the old materials volatile, or soluble, or removable, and this source of fuel is an economy of the machine; and when food is insufficient, or starvation occurs, it enables it to continue its work, using the products of its own structures and its own stores of fat as sources of power.

If the chemistry of repair is complicated and imperfectly understood, far more ignorance exists regarding the chemistry of development. The chemistry of the formation of the first blood-globules, the first nerve-cell, or muscular substance, or cartilage in the fœtus, will perhaps never be understood; but when once these substances are formed, it seems comparatively easy to comprehend that like produces like, although

this universal law is only a statement of the fact that nerve produces nerve, and muscle muscle, and bone bone, and furnishes no explanation whatever of the chemistry of development or of repair.

The clearest idea I can offer you at present is that each particle of the body must be considered as a ductless gland, having a contact action on the materials of repair brought to it, so that it separates the substances that can be changed into its own structure. If the fœtus would grow where the mammary gland exists, so that instead of milk being formed the fœtus would take from the blood just that which is required to form each structure and tissue of the body, you would on a great scale have a demonstration of the different chemical actions which are continually going on in the building up of each particle of our textures. Each portion of muscle, or nerve, or other tissue takes from the blood that which can nourish it, but in order that this nutrition may be effected not less than three different actions must simultaneously be going on.

First, the food must be brought; secondly, the chemical action of assimilation must take place; and thirdly, the old materials must be taken away. If the balance is not rightly kept between these mechanical and chemical actions, malformations and all degrees of wrong growth between hypertrophy and atrophy will occur.

I shall divide the diseases from the wrong action of one or of all these causes into two great classes; one I shall consider arises from pertrophic, and the other from subtrophic, chemical actions. Hypertrophy and atrophy constitute extreme cases of opposite actions in these two classes of disease.

In every machine the wear must be proportioned to the work, and the amount of repair required depends upon the wear. Hence, from the amount of work done, you may draw some judgment as to the amount of repair that is necessary. Helmholtz states that the best Austrian steam-engine can raise its own weight 2,700 feet in one hour; whilst he calculates from the pressure of the blood that the human heart

raises its own weight 20,250 feet in one hour; so that the human machine requires an amount of repair very much beyond that of a first-rate steam-engine, and errors of repair, pertrophic and subtrophic, must be ready at all times to occur.

In nutrition the first important condition is that nutritive substances should be brought to the spot where the action of assimilation is going on; this is effected primarily by the circulation through the blood-vessels, and secondly by diffusion of lymph into the structures. The third equally important condition is that the used substances should be taken away, and this also is effected primarily by the circulation through the blood-vessels, and secondly by the circulation through the lymphatics. As the circulation in the blood-vessels is under the regulating power of the nervous system, it follows that two out of the three simultaneous actions of nutrition are under the direct influence of the nerves.

There is as yet no evidence that the second necessary condition, that of assimilation, can be altered directly in quality or quantity by the nervous system. Indirectly, by lessening or increasing the amount of substances that go to or come from any part, the nerves can exert a potent influence on pertrophic or subtrophic actions; and indirectly, by altering the circulation, the nerves can exercise an influence on the peroxidation or suboxidation in any tissue, and thus the temperature at which the process of assimilation is carried on may be affected.

In the vegetable world, on account of the much greater variations of temperature that occur, it is easy to see how assimilation is influenced by heat. The tropical plants will grow in our light, provided the heat of the tropics is given to them here. If in the full light of the sun a plant could be kept all the year round at a temperature just above freezing little or no assimilation would take place.

In animals also the chemical actions of assimilation depend on the temperature; and the variation of a very few degrees makes a material difference in the chemical actions which take place in the textures.

In the present state of our knowledge it is not possible for

me to classify the different diseases that are produced by different errors of repair arising from errors of action in the different processes of nutrition. At some future time there will be a class of diseases arising from excess or deficiency of materials to be assimilated, another large class arising from wrong chemistry of assimilation itself, and another arising from excess or deficiency in the removal of materials that have been assimilated. Ultimately animal chemistry will enable us to make a far more perfect classification of pertrophic and subtrophic diseases than at present is possible; and now, from want of knowledge, more than from want of space, I shall take only one or two of these diseases of nutrition, and omitting any explanation of the wrong chemistry that produced the malformation and sets up the mechanical diseases, I shall again show you how secondary chemical diseases may arise from the mechanical errors which may be vastly more dangerous than the slight chemical errors by which the mechanical diseases were originally produced.

Perhaps two of the most striking examples that I can bring before you will be imperfect closure of the foramen ovale, and imperforate hymen—two opposite errors of development; the one depending on subtrophic and the other on pertrophic action. Each of these opposite chemical wrongs produces an opposite mechanical effect; and these mechanical diseases give rise to chemical disorders, which ultimately may stop the working of the machine. Imperfect closure of the foramen ovale and ductus Botalli produces general suboxidation, and imperforate hymen causes an absorption of poisonous products of decomposition, which affect and ultimately stop all the chemical actions of nutrition.

In the first disease the result of the subtrophic action is that a space between the two hearts is not filled up. The blood in consequence passes from the right to the left side, without going through the lungs. By this slight mechanical error, as it might seem, compared with the perfection of the rest of the machine, the whole chemistry of respiration is reduced to its lowest point. The absorption of oxygen is so diminished that the blood is not arterialised, and the carbonic

acid is not liberated. The chemical action that takes place outside the capillaries, on which the heat and the power of the body depend, is reduced below the average. Dr. Foster, in the 'Dublin Quarterly Journal,' August, 1863, mentions some experiments in two cases. In one, "the fingers were seldom more than 5° F. to 8°, the toes 1° to 3° higher than the temperature of the room. In the other the fingers were from 6° to 9°, the toes 2° to 4°. In the mouth in one the temperature was 96°, and in the other 97½°. In one it once fell as low as 90°, and in the other to 92° F." Even the chemistry of repair, by which the reformation of the different structures takes place, falls below the healthy amount. The body is weak, and wastes until premature death liberates the elements and allows the forces they possess to act with greater energy.

Thus, then, the results of this slight deficiency of nutritive action is general suboxidation from insufficient supply of oxygen to the blood and textures; and from this local passive congestions are apt everywhere to occur, and general subtrophic action is the final result.

The first chemical causes of the disease cannot be touched, and the mechanical complaint itself is not within reach; so that the symptoms and complications are alone capable of treatment, and as these proceed from suboxidation and subtrophic action, the mechanical and chemical promotion of oxidation and nutrition are the indications to be continually carried out. The oxidation may be promoted by constant attention to the warmth of the surface and by mechanical friction. Dr. Foster says that peroxide of hydrogen in eight minim doses three times daily improved the colour, made the breathing less laboured, and caused a rise of temperature. The subtrophic action may be palliated by warmth and friction, and also by reducing the work of the machine so far as to avoid all exhaustion. By giving the utmost external warmth, the minimum amount of the force set free in the body is required to be expended in keeping up the temperature of the body; and the greatest amount of force remains capable of conversion into motion in those muscles which are neces-

sary for circulation and respiration. If a part of the total force is spent in voluntary actions by strong exertion, the supply of power to the heart and lungs is so lessened that the tendency to passive congestions in the circulation is increased, and then mechanical obstructions, which constitute the most dangerous complications, are produced.

In contrast to this subtrophic disease, I will now shortly bring before you the pertrophic malformation of which I spoke to you, imperforate hymen. Whether a locally increased supply of nutriment leads to the excess of development perhaps will never be determined, but the mechanical wrong remains for years, producing no bad effects; and if menstruation did not take place, the original complaint might remain unknown throughout life. As soon as menstruation begins, the chemical secondary disease begins also. The excrementitious blood finds no means of escape. It remains within and undergoes chemical changes; products of disintegration, which chemistry has yet to determine, are formed. Those that are soluble are absorbed with the water of the effused blood; and month by month this process is repeated, until the blood and the textures are poisoned, and nutrition and oxidation are modified or stopped, and anæmia, debility, dropsy, and death may result.

With regard to the treatment of the symptoms and complications arising from the chemical disease, nothing need be said, because the mechanical disease can be got at. If it were otherwise, chemistry has no antidote for the poison, and as in uræmia or in jaundice, we should be able, perhaps, not to do much for the chemical cause of the complaint; but in imperforate hymen the slightest mechanical operation is all that is required to remove the mechanical obstruction, and then if no inflammation comes on, gradually the blood and textures recover their healthy composition, as no further poisoning takes place.

Instead of drawing my examples of the origin of chemical disease from malformations, I might show you that the same relationship exists by taking errors of reformation or repair. In nutrition pertrophic or subtrophic errors occur, and from

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these wrong mechanical and chemical actions arise, which may be far more serious than the original errors. In the three simultaneous actions that constitute nutrition, it is not always possible to separate the effects of each action in producing the error of nutrition; but in some cases it is possible to find more of one than of the other two actions, as in the following examples:—

First, let me bring before you chemical diseases of repair, arising chiefly from variations in the supply of nutriment.

Speaking of Hunter's well-known experiment, Mr. Paget says, "When the spur of a cock, for example, is transplanted from the leg to the comb, which abounds in blood, its growth is marvellously augmented, and it increases to a long, strange-looking mass of horny matter, such as is shown in two preparations in the Museum of the College. In one (54) the spur has grown in a spiral fashion till it is six inches long, and in the other (52) it is like a horn curved forwards and downwards, and its end needed to be often cut to enable the bird to bring his beak to the ground in feeding and to prevent injurious pressure on the side of the neck." If this mechanical pressure had not been removed by operation, it would probably have caused the death of the animal by obstruction or starvation. So that here is an instance of a pertrophy producing a serious mechanical complaint.

Instead of an excess of nutriment there may be a deficiency, and the subtrophy from the want of raw material may be rapidly fatal. I am again indebted to Mr. Paget for my illustrations. "A medical man wished to be bled in a fit of exceeding drunkenness, and some one bled him—bled him to three pints. He became very ill, and next day both his feet were mortified from the extremities of the toes to the instep."

One of Mr. Swan's donations to the College Museum is the larynx of a man who, while in low health, cut his throat, and suffered so great a loss of blood that the nutrition became impossible in one of those parts to which blood is sent with difficulty, and before he died his nose sloughed.

Secondly, I will mention states of pertrophy and subtrophy arising from the actions of assimilation going on in a part,

and I shall then show you the mechanical and chemical diseases produced from these altered states of nutrition.

I shall draw my examples here from enlargement of the uterus during pregnancy, because the first commencement of the increased growth does not depend primarily on the increased flow of blood, but on the changes in the uterus itself which determines that flow. The increased action in the uterus itself must be set up by the intense actions going on in the impregnated ovum, and by the internal mechanical pressure of the foreign substance in the uterus. As soon as the increased nutrition begins, the increased flow of blood follows, and keeps up the rapid formation of the different structures of which the uterus is composed. As soon as the pressure is removed, and more or less loss of blood has occurred, the structures cease to be nourished, and in a few weeks no trace of the increased nutrition can be found.

During the time of the greatest pressure very many different mechanical results may be produced, and thus mechanically very different secondary chemical diseases may arise. In speaking of tubular nephritis I have mentioned the obstruction of the renal veins in pregnancy, and the consequent production of Bright's disease and uræmia. Another most frequent chemical disease from the pressure is jaundice. More rarely gall-stones and all their tertiary mechanical agony occur. Another disease resulting from pressure is hæmorrhoids, and when these inflame great additional suffering is produced.

When the mechanical pressure in the act of delivery reaches an extreme height, then many more chemical diseases are produced. Of these I may mention a few, as sloughing of the soft parts; inflammation of the perineum from rupture; inflammation of the peritoneum from rupture of the uterus; rupture of the air-vesicles of the lungs and general emphysema of the cellular tissue; stoppage of the chemical action of respiration in the fœtus.

It is in the highest degree probable that by chemical agents the force of assimilation in the different textures may be increased or diminished in its action. Animal chemistry at

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present has hardly touched upon this subject, and I can only give you one or two examples, which, however, may serve to point out the vast and important field which is here open for future research. When I come to the classification of medicines I shall endeavour to show you that one grand class consists of those substances which promote or retard the chemical actions of nutrition—not by causing more or less blood to flow to any part, nor by hastening or retarding the removal of the used substances, but by increasing or diminishing the chemical actions which are concerned in assimilation.

The example which I will here mention of increased nutrition by the action of a chemical substance is for the chemist that invaluable fact that iron, even metallic iron, iron rust, or the finely-reduced metal itself, taken into the body produces an increase of blood-globules. Where and how this chemical action takes place chemistry cannot yet make out. The iron, when taken, is probably acted on by acids in the stomach, and is absorbed into the blood and diffused into every structure; but whether the colourless corpuscles in the lymph, the spleen, and the blood itself by the action of iron and oxygen form hæmoglobin cannot be determined. We know that lymph reddens when exposed to the air, and that in the spleen transitions from white to red corpuscles may be observed, and coloured cells and nuclei, which appear to be disintegrated blood-globules, may there be found mixed with products of oxidation—as uric acid, hypoxanthin, xanthin, leucin, tyrosin, inosit, volatile fatty acids (formic, acetic, butyric), lactic acid, many colouring matters, an albuminous substance containing iron, and generally very many iron compounds. This tells us very little as yet; but chemistry will some day say how and where the increase of hæmoglobin occurs when iron is taken. A somewhat similar, but less important example exists in the action of phosphate of lime and of carbonate of lime in increasing the growth of the bones in cases of rickets; and a well-known and often-applied theory exists that phosphorus when taken, not only in substance, but even as phosphoric acid, can increase the formation of nerve-substance; but for this there is at present not the smallest shadow of proof.

It has also been said that zinc is to the nerves what iron is to the blood ; but there is absolutely as yet no chemical evidence that zinc, or any salts of zinc, have any power over or take any part in the formation of nerve substance. Far more probable is it that zinc acts like lead, and perhaps silver, in retarding or stopping the chemical actions which are taking place in assimilation, and thus producing what I may be, perhaps, allowed to designate as a chemical disease.

One of the most striking instances of the action of a chemical substance in diminishing nutrition is seen in lead disease. The poison may be seen in the gums, and felt in the bowels, and be got out of the muscles of the arm ; and as three grains of sulphate of thallium, when given to a rabbit, could in six and a half hours show thallium distinctly in the aqueous extract of the lens, and as even two grains in six hours also gave there slight traces of thallium, there can be little doubt but a salt of lead passes everywhere—into the blood-globules, into the muscles, into the gums, and even into the lens of the eye, and that according to its power, and according to the actions going on in the parts, it exercises a greater or less influence upon the chemical changes which are taking place. In the voluntary and involuntary muscles the lead must either combine with the syntonin or be precipitated in it as an insoluble sulphuret, and so stop the chemical changes upon which the action of the muscles depends. It is highly probable that salts of lead act upon other textures; as, for example, on the young blood-globules, stopping the formation of hæmoglobin ; and on the sympathetic nerve, causing the violent pain of colic; also on the muscular coat of the small arteries, lessening their increased action, as when applied as a lotion in inflamed skin ; but on all these points chemistry must give us far more exact information than we at present possess. I might say the same for silver, arsenic, copper, and many other medicines.

The action of salts of silver in making the conjunctiva blue when applied as a lotion, and in making the skin permanently blue when it has been taken as medicine, shows how substances enter and act chemically in the textures. A grai

and a quarter of sulphide of silver was given to a guinea-pig in divided doses in the course of twelve days. The silver was found in the ashes of the liver, kidney, and stomach; less distinctly in the bile and the urine, still less in the lenses of the eye. It was not detectable in the ashes of the brain, probably because the quantity taken was too small.

The two diseases of repair which will best bring before you the origin of chemical and mechanical disorders are anæmia and lead paralysis, the one arising from the absence of iron and the other from the presence of lead.

The chemical diseases of subtrophy and suboxidation which are produced by anæmia are as opposite as dropsy and fatty degeneration. General debility, not only muscular and nervous weakness, but feeble growth and feeble production of heat, characterise anæmia. The pressure of the blood in the arteries becomes so feeble that the circulation stagnates in the capillaries, and the effused lymph in the cellular tissue tends to accumulate, not only in the lowest part of the body, but even in the lowest part of different organs.

Local congestions are ready to produce obstructions, around which the lowest degrees of peroxidation are set up, and the most feeble inflammations give rise to a fresh resistance, which is often more than the heart can overcome. In every texture the want of healthy change from imperfect supply of oxygen becomes evident, not only in the function of many organs, but even in the fatty formation and deposition which in anæmia rapidly adds to the general weakness and contributes to the subtrophic action which the deficiency of oxygen occasions.

Thirdly, I will show you the relationship of chemical to mechanical disease in the results of errors of excess or deficiency in the process of the removal of the assimilated materials.

That removal of a product does exercise an influence on its growth is evidenced in shaving the hair, or cutting the nails, or taking away the milk teeth; and within the organs it is highly probable that some medicines hasten the formation and removal of disintegrated substances. Thus oxygen, mercury,

iodine, and, indirectly, if not directly, alkalies increase the changes in the assimilated material, and, as in the example of mercury, may set up so rapid an action that peroxidation, even as evidenced by all the phenomena of inflammation, may be produced.

Moreover, errors of deficiency of removal may give rise to chemical diseases, from which mechanical disorders may follow. Lead palsy, again, well illustrates this, and shows also the relationship that exists between the chemical actions of assimilation and removal, for the poison stops both processes, and thereby produces a loss of mechanical power, which is seen in the inability of the muscles of the forearm to support the weight of the hand.

The three actions of supply, assimilation, and removal which constitute nutrition are usually so closely dependent and interwoven that no separation between them can be made, and the result of these actions, whether in excess or in deficiency, may each be summed up in a single word. For example, an increased supply of blood, increased assimilation, and slightly increased removal, constitute hypertrophy. Whilst the diminished supply, and lessened chemical action, and more or less diminished removal of disintegrated matter produce simple atrophy, or atrophy with more or less degeneration, according to the nature of the substances (as, for instance, fatty and calcareous matters) which remain unremoved in consequence of the suboxidation occasioned by the diminished supply of blood.

I shall now take the conjoint effect of these three actions, and I shall try to bring before you one or two chemical diseases and the secondary mechanical disorders which are thereby produced.

Among many diseases from which I may select, I shall take simple hypertrophy of the prostate on account of the very marked mechanical disease which springs from the primary chemical error of nutrition.

"Simple enlargement of the prostate," says Mr. Paget, "consists of increased gland cells and muscular fibres with masses of new-formed tissue within and without the gland.

These prostate glandular tumours are composed of simple tissues like those of the gland itself. The gland cells and muscular fibres are not to be distinguished from those of the gland itself. They are masses of new structure, resembling the prostate embedded in the proper substance of the enlarged gland. Near the enlarged prostate similar detached outlying masses of new substance like tumours in their shape and relations, and like prostate gland in tissue, may sometimes be found. A very large specimen was taken from a man, 64 years old, and who for the last four years of his life was unable to pass his urine without the help of a catheter. He died with bronchitis; and a tumour, measuring $2\frac{1}{2}$ inches by $1\frac{1}{2}$, was found lying loose in the bladder, only connected to it by a pedicle moving on this like a hinge, and when pressed forward obstructing the orifice of the urethra. Now, both in general aspect and in microscopic structure this tumour is so like a portion of enlarged prostate gland that I know no character by which to distinguish them."

The immediate result of this growth is that the urine cannot flow out; it is mechanically stopped in a greater or less degree, according to the amount of the impediment. The mechanical disease then begins to produce its effects. These are altered pressure of the urine on the bladder and altered chemistry, in consequence of more or less of the urine being retained in the bladder.

In a previous lecture I have brought before you the phenomena of the fermentation of the urine. Even in perfect health, whilst the urine is in the bladder, chemical changes may be going on, although they usually escape our notice; but when a little of the urine is continually left in the bladder, then the internal chemical action becomes very evident. The increase of time during which the ferment can act on the urea, the production of vibrios, the increased chemical action going on in the prostate, these sometimes very slowly, sometimes very rapidly, according partly to the amount of acid that passes from the kidneys, set up ammoniacal urine, and then the chemical action of carbonate of ammonia on the urine and on the mucous membrane has to be added to the original chemical disease.

Meanwhile the mechanical pressure of the urine has been more or less effective, and helps to increase the chemical action on the mucous membrane. Each time the bladder contracts the pressure temporarily rises in intensity, and slowly increased nutrition of the different tissues and increased oxidation in them is set up; this insensibly passes into peroxidation, and the chemical action of the carbonate of ammonia not only adds to the inflammation, but alters its products, so that mucus and pus can no longer be recognised, but a gluey, ropy, adhesive matter, even more adhesive than the stringy alkaline secretion from the throat and nose, is produced. The ammoniaco-magnesian phosphate crystallises in and upon this matter, and the granular phosphate of lime increases its consistence, so that a mechanical irritation, or even a fresh mechanical obstruction to the passage of the urine, is added to the fearful sufferings which a small chemical error of hypertrophy originally set up.

If you look at the treatment of this disease, you will soon see how the mechanical secondary disorder constitutes the important part of the complaint. Without a mechanical remedy almost no good whatever can be done by treatment, and when the catheter is used scarcely any other treatment is required.

During the gradual increase of the hypertrophy an increased action may suddenly come on from internal or external causes; for example, from excessive acid or other chemical irritant formed in the kidneys and passing into the bladder; from cold applied to the skin; or from substances in the blood passing into the structure of the prostate, increased flow of blood to the hypertrophied part may take place, and this may reach to any amount of congestion and inflammation; an immediate stoppage of the flow of water is the result, and when this happens, recourse must be had the same day to mechanical relief, and very often from that date the catheter must be always passed, more or less frequently, according to the degree of wrong chemistry that exists. If the ammoniacal urine be not drawn off sufficiently often, diffusion takes place into, and even through, the mucous membrane of the

bladder. The phosphatic salts are found not only adherent to the bladder, but even deep in the structure of the mucous membrane. The putrid urine passes through into the blood, and thereby a general state of poisoning may be produced. This has been also called uræmia, and by some persons ammoniæmia, but the experiments of Hammond, in the 'American Quarterly Journal of Medical Science,' vol. xli., p. 55, 1861, show that putrid urine acts much stronger as a poison than carbonate of ammonia, and it is highly probable that among the offensive matters in putrid urine some more poisonous substance than carbonate of ammonia or urea may be formed. Certainly the poison differs from those higher compounds which cause death in the so-called uræmia of Bright's disease.

If, instead of hypertrophy, I take an example from atrophy, which depends on diminished supply and lessened chemical action, and more or less diminished removal of disintegrated matter, you will see an opposite chemical error of nutrition, giving rise to secondary mechanical or chemical diseases far more serious than the primary complaint.

I will shortly bring before you senile gangrene and apoplexy from diseased blood-vessels, both of which arise from a slowly-acting error of nutrition, suddenly giving rise to a chemical or mechanical disease, which often rapidly ends in death, or when this is not immediately produced, the effect of the diseases in causing general or local loss of power is only very partially removed.

No part of the body is exposed to greater continuous action in proportion to the supply of blood to its structures than the arteries. From the semilunar valves to the arterial capillaries the structures of the blood-vessels are exposed to mechanical pressure comparable with the pressure of the atmosphere. Thus in man the pressure in the aorta is equal to one-third the weight of the atmosphere. It has been found to be 9·7 inches of mercury. In the brachial artery it is equal to one-sixth, or 4·5 inches of mercury. Down to the capillaries this pressure is continuous, lessened by the friction of the blood in the vessels. This pressure and friction have a direct

influence on the chemical actions of nutrition and oxidation which take place in the coats of the arteries. When the pressure in the arteries is increased, the actions of nutrition and oxidation must be increased also, and with long-continued action a state of pertrophic action and peroxidation must be produced, giving rise to thickenings of the different coats, which entirely alter the chemical changes going on in them. Hence errors of disintegration arise, and then suboxidation and subtrophic action readily occur. The acids that ought to be produced to dissolve the earthy matters are no longer formed; the fatty matters no longer are oxidised, and hence fatty and earthy substances accumulate, and the healthy tissues are not formed. If the nutritive fluid be loaded with fatty matter, or if the supply of oxygen be deficient from any cause, or if the conditions on which the oxidising and nutritive actions depend be lowered, the errors of disintegration will more rapidly arise.

Wherever the arterial textures are injured or destroyed, there the mechanical pressure from within is less capable of being resisted, and rupture is ready to occur at the place of least resistance, and when any slight extra pressure is made the vessel breaks. If this happens in the brain a mechanical blow and a rupture of the nervous structures is produced, and paralysis is the result, the muscles being cut off from the action of the will. When the rupture is large, and the quantity of blood effused great, the pressure on the nerves that regulate the motions of the heart and muscles of respiration may quickly put an end to life.

When the smallest branches of the arteries are much thickened, the supply of nutritive materials and of oxygen to the textures beyond these arteries is interrupted. The day before the senile gangrene begins, the arteries supplying the part are nearly, if not quite as diseased as the day after when the mortification has commenced. The altered action in the textures begins only when the diminution of nutritive material has reached to a degree that alters the chemical actions of the part, or when the diminished amount of oxygen produces the same effect. From one or other or

from both of these causes the part becomes livid, and gradually darkens until it becomes black; as the oxidation is stopping it becomes cold, and the accumulation of carbonic acid and the stoppage of the circulation render the nerves insensible. The stagnant blood exudes its serum under the cuticle, where there is least resistance, and the fluids, gradually evaporating, leave a black-brown mass in which vibrios are produced, and putrefaction is set up, varying in its products with the dryness and the temperature of the part.

The further a part is from the centre of the circulation, the more the force of the blood is diminished by friction, and the more readily will the altered vessels cause gangrene to be set up. Thus the extremities are the seat of the disease, and in the toes the greatest loss of chemical action takes place. Around the dead part the obstruction causes an opposite action; increased flow of blood and increased chemical action, amounting even to inflammation, occurs. At the part where the dead nerve joins the living structures the most violent pain may be produced, and this become so severe that perfect rest and the strongest opiates alone give any relief. The progress of the mortification can only be stopped by keeping up the temperature, promoting the circulation by position, and making the blood as abundantly nutritious as possible.

Very much less serious errors of repair than those which I have mentioned may produce most remarkable general and local chemical diseases. Debilitating climates and hereditary subtrophic actions give rise to results at places of greatest pressure and least resistance, which, but for the striking phenomenon produced, might almost escape notice. In such a structure as the kidney it might almost be expected that from the immense pressure in the arterial vessels albumen, if not blood-globules, would constantly be forced through the dialysing membrane. In the renal artery the pressure cannot be much less than one-sixth of the weight of the atmosphere, and a considerable portion of this falls on the malpighian tuft, and has to be resisted by the walls of the vessel which separate the blood from the urine. If by subtrophic action this membrane is made less resisting, albumen may be forced

through; when the pressure is increased, blood-globules may pass into the urine; and when the pressure is diminished, the blood-globules first, and then the albumen, may disappear. So also in other parts of the kidney, where there is less pressure than in the tufts, as in the capillaries on the tubes in the medullary structure, a subtrophic action in the textures may allow an increased pressure in the capillaries to force out substances which would not escape if the dialysing membrane were thicker. From one or other of these places fat, albumen, and blood-globules may pass into the urine, and constitute the complaint known as chylous urine, which is worthy of a few minutes' attention, not only as an example how increased pressure can produce wrong chemistry of the urine, but also because it furnishes the most striking contrast to Bright's disease in its course, and in its secondary diseases.

In chylous urine the daily loss of albumen may be as much, or even considerably more, than in Bright's disease, and yet the complaint may last for a quarter of a century, whilst the patient may continue his work, and, if he were blind, might know nothing of his ailment except by a feeling of more or less general debility. No secondary diseases are produced, no accidents occur, except that sometimes so much fibrin may escape from the blood into the urine that it may cause the contents of the bladder to coagulate, and thus give rise to a mechanical impediment to the escape of the urine. The distention and obstruction may cause much pain and distress for a day or two until the clot shrinks, and the fibrin loses its cohesion and gradually breaks up and is passed away in the urine. Throughout the course of the disease there is usually no dropsy and no uræmia. The poisoning of the blood, which commences with the alteration of the different structures in Bright's disease, never takes place in chylous urine. The structure of the kidneys may let one or many of the constituents of the blood out when the pressure is increased, but the alteration does not keep the uringenous substances in the blood.

In the 'Medico-Chirurgical Transactions' for 1850 you will find the history of a patient who has now been under my

observation more or less frequently for sixteen years. I shall here only bring before you the evidence of the effect of pressure in causing the altered chemistry of the urine.

The first specimen of the urine I saw "was made at 9.30 a.m., one hour and a-half after breakfast, the patient remaining in bed. It was clear, acid to test paper, not light coloured; sp. gr. 1022·5. It did not coagulate when boiled nor when nitric acid was added; but the acid made the colour deeper. On the surface there was a slight appearance of oil; one or two blood-globules were also seen." "The second specimen was passed at 11.30 a.m., two hours after he had got up. It was of a yellowish-milk colour, quite thick, and spontaneously coagulated, so that it could not be poured from the bottle. The specific gravity was 1017·0. It was very feebly acid to test paper. Nitric acid and heat gave a considerable precipitate. Under the microscope I saw blood-globules in some quantity. No trace of oil-globules, but a large quantity of very minute molecular matter, scarcely resolvable by a magnifying power of 320 times. No trace of casts of the ducts could anywhere be found. Little films of coagulum could be seen, containing many blood-globules. Treated with ether, the ethereal solution was clear; the urine below was cloudy, but on long standing became clear. The ethereal solution on evaporation gave a great mass of oil-globules, but with the microscope no decidedly crystalline fat was seen."

In the 'Philosophical Transactions,' Part II. (1850), you may see some further experiments on the influence of rest and motion on this patient in lessening or increasing the albumen in the urine previous to or after food was taken :—

Last food was taken at 5.15 p.m. yesterday. He lay in bed this morning till 9.30 a.m.

10 p.m. last night.—Urine milky.

6.40 a.m.—Urine yellow, slightly milky, acid, contained a little albumen.

8.10 a.m.—Urine clear, healthy-looking, made just before breakfast, which consisted of boiled milk (a pint), with sago and bread with a little butter; the specific gravity of the urine was 1021·3; it gave no coagulum with heat and acid.

9.30 a.m.—Urine opalescent, but not spontaneously coagulable; specific gravity 1019·0; gave a considerable precipitation of albumen with heat and acid.

12.30 a.m.—Urine milky; spontaneously coagulated.

Contrast this with the following day, when he got up earlier and breakfasted as before, though half an hour later:—

Last food was taken between 5 and 6 yesterday. He got up this morning at 6 a.m.

10 p.m. last night.—Urine milky.

2 a.m.—Yellow milky urine, acid, slightly coagulating with heat and acid.

6 a.m.—Urine quite clear, healthy-looking, acid, contained no trace of albumen; specific gravity 1026·4.

7.30 a.m.—Urine opalescent, feebly acid. Gave a large precipitate of albumen with heat and acid; contained multitudes of healthy blood-globules, but no casts. Specific gravity, 1018·8.

9 a.m.—Urine opalescent; by 12 became a solid jelly, alkaline. This was passed just before breakfast.

11.30 a.m.—The urine coagulated spontaneously to a strong unclear, slightly milky jelly.

Experiments on other days gave the same results, showing that when he remained in bed the urine was clear, and did not contain albumen, and when he got up the albumen, fibrin, and blood-globules passed into the urine even when no food was taken; so that I frequently determined beforehand whether the urine before breakfast should be albuminous or not by directing the patient to get up and move about early, or to keep very quiet in bed. And by keeping him in bed all the day the urine throughout the whole day was very slightly albuminous.

Fifteen years after these experiments I have the following note:—

4 p.m.—Very milky urine. Specific gravity, 1031.

10.30 p.m.—Urine has slight milkiness. Specific gravity, 1029·5.

6.40 a.m.—Clear urine; specific gravity, 1020; contains no trace of albumen.

8.30.—Breakfast; up early.

9.15 a.m.—Urine clear; considerable precipitate with heat and acid. Specific gravity, 1023·0.

This influence of rest and of motion indicates to me that this disease depends on some slight alteration in the structure of the kidney, dependent upon some slight change of nutrition, which remains without perfect repair for years. Even with a slight increase of pressure the altered mechanical condition immediately affects the chemistry of the urine, and this to a degree resembling the wrong chemistry of the most serious Bright's disease, but none of the complications of Bright's disease occur; and sometimes, without any assignable reason whatever, or by the aid of strong astringent medicines, as gallic acid in large doses, the wrong chemistry will entirely disappear, and for a time at least the dialysing membrane appears to be sufficient to resist any pressure that it has to bear without admitting any of the proper constituents of the blood to pass through.

In order to show you how vast this subject of errors of chemical repair is, I must very briefly close this lecture with a sketch of one other chemical disorder arising from the injurious action of a chemical substance affecting the growth of the epithelial textures of the body. I allude to chimney-sweep's cancer produced by the action of soot.

The most violent opponent of spontaneous generation never can believe that any germ passes in with the soot, nor is it conceivable that any nervous or vascular action can transform an epithelium cell into a cancer cell. Whether the epithelial cancer be superficial in the rete mucosum, or deep, commencing in the epithelium of the sebaceous or sweat glands of the scrotum, or in the epithelium of the hair tubes, it consists in no error of oxidation, but in an entire change in the chemical growth of an epithelial cell.

It was for a time considered that a characteristic form of cell, a so-called cancer cell, marked this altered growth; then it was believed that an error *loci*, a peculiar birth-place, gave rise to it. The cellular tissue produced it. A corpuscule of the cellular tissue became an epithelial cancer cell. Most recently Dr. Thiersch has stated that the disease comes from

the loss of the right balance of pressure between the epithelium and the stroma of the skin. The necessary equilibrium is destroyed by insufficient growth of the stroma; this gives rise to the peculiar increased development of the epithelium.

Although any peculiarity of form as characteristic of the cancer cell is given up, and we no longer recognize it by its fusiform, caudate, multinucleated, or polygonal shape, yet it is by no means unlikely that chemistry will detect some peculiarity of composition; for the growth, propagation, and consequences of an epithelial cancer cell prove that it differs from an ordinary epithelial cell; and this difference of action probably is connected with some difference in chemical composition.

Not only does the soot act on the scrotum, but it even acts on the hand, and the pressure of a pipe on the lip or of a finger and thumb during shaving, and the lessened actions of declining years, all may lead to an altered epithelial cell growth. The cells no longer become healthy texture, but, like pus cells, they grow and multiply and oxidize and decay. Wherever a cancer cell forms it begins its increased chemical action of nutrition, and it easily sets up peroxidation, and this adds the effect of ordinary inflammation to the altered nutrition of the part. At first, or indeed at any time, the increased flow of blood may cause all or any of the healthy structures to increase; thus the epithelium, the papillæ, the blood-vessels may grow or waste, according as the nutritive fluid is attracted by growth or retarded by pressure. Even in the arteries themselves these changes may be observed, the inner epithelial coat may become thickened. The middle muscular coat may be still more developed and the outer coat of thickened cellular tissue may be extremely enlarged; after long-continued pressure the outer coat may become fatty; the form of the vessel may be so changed that it becomes triangular instead of round. Generation presses on generation, and the multiplied growth exerts a pressure on all the neighbouring textures; so that increased action is accompanied in places by decreased action, and disintegration and suboxidations occur. The pressure destroys not only the healthy increased growths,

but the very cancer cells themselves, so that they waste away, in the places of greatest pressure, and become horny, fatty, or even earthy before they entirely disappear.

The abnormal growth takes the place of the healthy structures, and more especially in the deep-seated form of epithelial cancer, a single cell, or possibly even a nucleus, or a granule, or a particle of matter that can become a cell, grows into an afferent lymphatic vessel, and is immediately carried to the gland. There it is stopped, and there it goes through the same series of actions as it would have gone through in the skin—at first, pertrophic and peroxidizing actions, to be followed by subtrophic and suboxidized results, whilst rapid increase of epithelial and cellular growth goes on until some particle spreads into the efferent lymphatic, from whence it passes to any organ, and sets up a new colony, going through the same cycle of actions as it would have gone through in the skin.

At present, no medicine is known which can keep up the healthy formation of the epithelial texture, or which is able to stop the too prolific growth of the cancer cells. The chemical or mechanical removal of every outlying cancer cell alone can afford a respite, and in a very few cases of epithelial cancer may give a perfect cure of the disease.

PART V.

ON MECHANICAL DISEASES AND THE SECONDARY CHEMICAL DISEASES THEY PRODUCE.

LECTURE XIV.

ON SURGICAL DISEASES; FRACTURES, DISLOCATIONS, RUPTURES, &c.; AND ON MEDICAL ACCIDENTS.

In my previous lectures I have shown you that chemical diseases are the parents of mechanical diseases, and I have frequently had occasion to point out how a secondary mechanical complaint sets up a more serious tertiary chemical disease than the primary chemical wrong, of which renal or biliary calculus are two most striking examples. I shall now endeavour once more to bring before you the compound or mechanico-chemical or chemico-mechanical nature of the actions in disease by taking an illustration or two from a vast number of instances which, in the subdivision of labour, fall under the care of the surgeon instead of the physician.

If I were a surgeon, I could give you a long course of lectures on mechanical diseases and the secondary chemical diseases which they produce, and on mechanical treatment and on the consequent beneficial alterations thereby produced in the chemical actions going on in the body.

The purest portion of pure surgery consists in the treatment of mechanical accidents and the increased or diminished chemical actions produced by the mechanical wrong. How important the relationship of the chemical to the mechanical effect is, may be seen in the fact that surgical accidents would, speaking generally, be free from danger, if it were not for the secondary chemical actions which necessarily come out of them and often rise to fatal diseases.

I might take my illustrations from fractures of the bones or

from rupture of the tendons, vessels, or membranes; or from dislocations, as of the joints or viscera, as in hernia; or from wounds, as of the skin, vessels, muscles, or nerves.

By any of these different mechanical accidents, I might show you the danger of secondary chemical disease; and if it were desirable to extend this long list of mechanical disturbances, I might take parturition, with all its accidents and consequences, to prove the origin of chemical from mechanical complaints.

You must not suppose that in this lecture I take my illustrations from surgery and midwifery, because medicine will furnish me with no examples sufficiently striking to be brought before you; on the contrary, in medicine also mechanical complaints abound—medical accidents, if I may so call them, among which I may mention obstructions, hæmorrhages, ruptures of valves connected with the heart, causing dilatation and hypertrophy; dilatation of the veins; emphysema of the lungs, and many other diseases. In addition to the surgical accidents, I shall bring before you one or two of these sudden or slow medical accidents to prove to you the connection of mechanical with chemical disease, or, if you please, of surgery with medicine.

From the immense variety and amount of mechanical diseases to which he ministers, and from the greater use he makes of mechanical remedies, the surgeon may be regarded as the mechanical physician; but in consequence of the secondary chemical diseases that are set up, he requires the same knowledge of chemical remedies as the physician who, in the treatment of disease, can use comparatively no mechanical remedies whatever, except rest. This comparative limitation to one class of remedies enables the physician to become more skilled in their use against the innumerable multitude of chemical diseases that he is called upon to treat.

My first illustration of the production of chemical disease by previous mechanical action will be taken from a compound fracture of the leg—in other words, fracture of the bone, with laceration of the muscles, blood-vessels, and skin at the same

time. When the same amount of injury is done to the bone, muscles, and blood-vessels, the skin remaining unhurt, the accident is, comparatively speaking, slight. Hence the amount of mechanical injury cannot be the cause of the seriousness of the compound fracture ; for a broken skin could not in itself make the difference of danger between a simple and a compound fracture. The difference really consists in the secondary chemical diseases which are set up in the two accidents. In the simple fracture, when perfect rest is possible, moderate peroxidation and pertrophic action only occur, and generally no formation of pus takes place. In the compound fracture the admission of the air to the injured parts is sure to determine excessive local peroxidation, and pus is much more likely to be formed, and this suppuration from the position of the wound, and from the access by the air of infusorial germs, or from the peculiar condition of the albumen, rapidly sets up decomposition. A state of general peroxidation is readily produced in the system, and not unfrequently the pus enters the blood, and becomes itself a species of ferment, modifies the peroxidation in the system, and, when it lodges mechanically (embolically) in different organs, it there becomes the nucleus and cause of a local modified peroxidation, which gives rise to secondary abscesses wherever the lodgment is effected. Hence increased oxidation and altered nutrition are the chemical complaints produced by this mechanical accident.

The first and most necessary part of the surgeon's treatment is to put the fracture in that position in which no fresh mechanical disturbance can take place ; then, by chemical means, lotions, and diet, he lessens or increases the chemical action, and day by day he carefully removes the foul matter, which is apt to become a chemical poison, and then not only interferes with the healing process, but, if absorbed, poisons the whole system.

If the general peroxidation should become excessive, and if the drain of matter should endanger life, the surgeon is then obliged to use mechanical instead of chemical treatment. He removes the limb with the knife. Thus a clean surface is gained instead of a foul one, and chemical and mechanical

irritation is removed, and moderate oxidation and nutrition soon close the wound.

My second illustration of the production of chemical disease by a mechanical action will be taken from dislocations. A dislocation is a mechanical misplacement, as, for example, of the bones; but it may also occur in the viscera, as with the uterus or the bowels. In this last instance it constitutes hernia.

In all severe dislocations of the joints the mechanical injury that is done to the parts around the joint causes more anxiety to the surgeon than the misplacement of the bones. The capsule, the ligaments, the vessels in the neighbourhood, may be so injured that violent inflammation may be set up; in other words, great alteration of the chemical actions of oxidation and nutrition around the joint may occur. The motion may be completely lost either by the formation of pus within the joint, or it may be only more or less hindered by the effusion of lymph in the surrounding textures.

When the dislocation accidentally remains unreduced the mechanical pressure may cause so much inflammation that the displaced bone may become so fixed that no motion may be possible.

When the surgeon is called to remedy the accident, he applies mechanical force in the opposite direction to that force that caused the dislocation. He counteracts the displacing force, the tension of the muscles, and the contraction of the tendons, and then, by rest and by remedies, cold lotions, salines, and aperients and diet, he tries to prevent the occurrence of increased chemical action.

He saves the joint, and ultimately the use of the limb is restored. Whilst if the dislocation has been neglected, he counteracts a very small part of the original mechanical injury and of the results of the chemical actions set up around the displaced bone by means of constant and long-continued mechanical motion of the limb, whereby a greater or a less amount of motion by means of a false joint is obtained.

But you will see better in a case of hernia how chemical

actions arise from mechanical injuries and how they add to the distress and danger which the accident occasions.

Usually constant mechanical pressure with a truss prevents any accident to the bowel, but when from a mechanical cough or from a jar displacement occurs, then mechanical pressure must be used by the patient or by the surgeon to return the bowel and to prevent the occurrence of any secondary chemical wrong action. When the hernia cannot be reduced, the mechanical strangulation immediately begins to affect the progress of the chemical actions in the part.

The entrance and escape of the supply of blood to the bowel may be so stopped that no oxygen may go in and no carbonic acid may come out. The action of the oxygen on the fuel may be so diminished that the chemical conditions necessary for producing mortification may occur, and to prevent the death of the intestine the surgeon, as soon as he finds that the pressure cannot be otherwise removed, mechanically divides the stricture. Then if the operation has not been too long delayed the circulation is restored and healthy chemical actions again take place, unless the chemical changes that have occurred in the bowel during the extreme pressure preclude all healthy action.

When the mechanical work of the surgeon is done, he then by perfect rest to the body and rest to the bowel, by the least amount of pressure of the general and local circulation, by diet, by lotions, and by medicines, endeavours to stop the increased chemical action which, under the name either of peritonitis or of diffuse cellular inflammation, is so apt to deprive him of the credit of his handicraft, and his patient of his life.

In every one of the mechanical injuries which may be brought to the surgeon, this relationship of the chemical disease to the mechanical accident is always in his mind. In some slight accidents, or in some parts of the body, the mechanical injury may hardly visibly alter the healthy chemical actions of oxidation and nutrition; but a disturbance always takes place; and in some parts of the body, from the nature of the textures or from the mode in which the nutriment and

oxygen are supplied, and the products of change and disintegration are removed, a very slight mechanical cause may give rise to a very great chemical effect.

Of all wounds, why are scalp wounds the most serious? Not surely because of the nature of the mechanical injuries themselves, but on account of the secondary chemical results which from the anatomical structure of the parts are more apt to occur in these than in most other kinds of wounds.

The two chemical consequences of scalp wounds generally are diffuse inflammation (peroxidation and altered nutrition), consequent on the looseness of the structure of the cellular tissue of the scalp; and necrosis or chemical death of the bone, which occurs when the periosteum which supplies the bone with food and oxygen is torn away by the mechanical injury.

As soon as the peroxidation begins in one spot of the cellular tissue it rapidly sets up similar action in the adjoining healthy texture, and causes the healthy oxidation going on in it to rise in degree until it becomes capable of increasing the oxidation in the neighbouring cells and structures, and so the inflammation spreads, and altered actions of nutrition occur. These altered chemical actions might extend through the whole cellular tissue of the scalp if the surgeon did not mechanically divide the tense skin, which relieves the pressure and the circulation, and allows the products of the inflammation to escape freely from the inflamed part.

So, also, when more or less of the surface of the bone is mechanically deprived of its nutriment, the part so injured immediately begins to go through changes of anoxidation and atrophy; whilst around the obstruction increased circulation is set up, and increased chemical action, which would slowly end in the removal of the dead and sometimes decomposed bone. The surgeon, by the removal of the dead bone, mechanically does what nature would do chemically, and by so doing he rapidly puts an end to a state of chemistry which, when left to its course, ends not unfrequently by the absorption of pus, in a general poisoning of the system, and a stoppage of all the actions which constitute life.

In another very large class of diseases—those, namely, which follow child-birth, the same relationship between mechanical injury and altered chemical action may be shown to obtain.

The removal of the child from the uterus may be regarded as a mechanical accident, an operation performed by nature; and violent mechanical injuries are often inflicted on the mother and child in the process of parturition. Thus by pressure, for example, rupture of blood-vessels and other textures between the uterus and placenta invariably occur, and accidentally other ruptures take place. Thus rupture of the perineum not unfrequently happens, and rupture of the bladder or even of the uterus itself more rarely occurs. The rupture of the vessels connecting the uterus and the placenta, and a transverse rupture of the uretus, cause oftentimes such hæmorrhage that an acute state of anæmia is rapidly produced; and the actions of oxidation and nutrition so suddenly decrease in consequence of the deficiency of the supply of oxygenated blood to the nerves and muscles that they cease to act, and death rapidly ensues. When the rupture of the uterus is longitudinal, there is less hæmorrhage, and in some rare cases a fatal result does not ensue.

Rupture of the perineum is slight or serious according to the degree of the mechanical accident. In slight cases healthy increased chemical action soon closes the wound, and little or no inconvenience is produced. In more extensive ruptures more serious wrong chemical actions arise, mortification, inflammation, and passage of the fæces into the inflamed false opening keeping up constant irritation. These evil effects may last through life unless by skilful mechanical treatment the surgeon can enable nature to close the opening which the mechanical force originally produced.

Among the diseases which have been classed together under the term puerperal fever you will find not only the best illustrations of the relationship of chemical to mechanical diseases, but also the best possible example of the close connection that exists between the actions that constitute fever and those that constitute inflammation.

At the time of child-birth the whole of the chemical and

mechanical actions going on in the body are suddenly disturbed. The whole oxidation and nutrition that was going on in and through the uterus is suddenly checked. An entirely new set of chemical and nutritive actions are beginning to be set up in the mammary glands. Each structure of which the uterus is made up is undergoing more or less altered action. The peritoneum has been stretched to the uttermost, and then is suddenly squeezed up. The muscular structure of the uterus has suddenly been called into the most intense action, and then suddenly has its violent action stopped, and its substance gradually dwindles, by oxidation and altered nutrition, away. The mucous membrane is not only bruised, but is torn, and has to be repaired and absorbed. Even the blood-vessels of the uterus are torn, and have to be closed and gradually to undergo that change of texture which reduces them to a small fraction of the size to which a short time previously they had attained. Without any inoculable products of inflammation being brought to the uterus by the accoucheur or nurse inflammation may be set up by spontaneous development from cold, from unhealthiness, from physical or mental distress. The inflammation may be most intense in one or in all of the uterine structures, and according to the different textures involved different names have been given to the resulting chemical disease.

If the inflammation is most intense in the peritoneum, the disease is called puerperal peritonitis. If in the veins, it is called puerperal phlebitis, and cases of inflammation of the absorbents have probably been included in this designation. When the symptoms are less manifest in the peritoneum and veins, the inflammation then is in the mucous and muscular structure, and when less distinctly localized, it is designated as puerperal fever, which in all cases is a spontaneous or inoculated inflammation of one or many of the textures of the womb just after delivery, when all the forces in the body are in a state of very great disturbance.

The effects of pressure upon the child in parturition are in the highest degree mechanical and dangerous. It may be mechanically strangled, or suffocated, or crushed ; it may be

so wedged in that it must either be removed in pieces, or the mother must be opened to get it out. No stronger proof of the energy and extent of the chemical actions of oxidation and nutrition that go on within us can be given than that they should be able to continue in action during the violent mechanical accident to which we are exposed at the end of the ninth month of our existence.

The pure surgeon considers that all these accidents of parturition do not belong to his handicraft, and the division of labour has almost taken them from the pure physician, and has given them to a separate class. But the amount of skill that is required to obviate and to remedy these mechanical accidents, and the amount of judgment and knowledge that the skilful treatment of the secondary chemical diseases requires, shows that no distinction can be drawn in the relative requirements of those who practise any one of the three branches of our profession. All should possess the same chemical and mechanical knowledge, while the handicraft can be neglected by the physician alone, who, to compensate for this loss of power, should possess the greatest insight into the chemical and mechanical forces that are in action in health and in disease. Even in the treatment of medical accidents no handicraft is of use to the physician. Whether these accidents are sudden or slow, generally speaking, no mechanical treatment can touch the cause of the evil. The physician may palliate or cure by mechanical and chemical remedies the secondary chemical diseases that may be set up; but no direct mechanical treatment of the original injury is possible, except that which can be obtained by rest.

The number of mechanical accidents which fall under the care of the physician is far greater than at first sight you would suppose. Some of them closely approximate to surgical accidents; for example, how slight is the difference between intussusception and inguinal hernia! How closely do different diseases of obstruction resemble surgical accidents! I might give you a long course of lectures on different obstructions, and on the secondary chemical diseases to which they gave rise. Then there are mechanical diseases of internal

ruptures, as of the semilunar valves of the heart, or of healthy or diseased vessels, constituting the large class of hæmorrhages. Then there are more chronic mechanical diseases, as emphysema of the lungs, dilatation of the bladder in some rare cases, varicose veins continually. I might almost include in mechanical medical accidents the large class of embolic diseases, but these arise from a slight antecedent chemical wrong, and are therefore, like calculi, primarily chemical, secondarily mechanical, and tertiary chemical diseases again; and as I have already said, these tertiary chemical diseases are far more dangerous than the primary chemical causes of these complaints.

Of these medical accidents I will take one a quick and the other a slow mechanical disease, to show you again how mechanical wrong action sets up chemical complaints.

I will read you a few short notes of a case of mechanical rupture of the aortic valves which I saw in St. George's Hospital. It is recorded in Dr. Latham's work, 'On the Diseases of the Heart,' vol. ii., p. 193.

"A stableman at Anderson's, twenty-eight years of age, was admitted into St. George's Hospital. He was suffering, and had suffered for twelve months, from severe palpitation of the heart, and was able to mark distinctly the moment of its commencement. It was one day just after running a horse down the yard to show off his paces to a purchaser. He had never had acute rheumatism. His lips were blue, his breath short, and his left side was painful. He had a dry cough. His bowels were confined and his urine free. It was ten weeks before his admission that his cough and dyspnœa had begun to be particularly distressing. Auscultation found dulness in the præcordial region, over an extent of four inches square. The heart's impulse increased, and its first sound prolonged, with a low blowing endocardial murmur over the aortic valves, and its second sound indistinct. He was bled three times under the urgency of his cough and dyspnœa. These, however, continued to increase. Five weeks after his admission his legs became œdematous, and in two weeks more he died.

"On examination after death three pints of fluid were found

in the right pleura, and the heart was enormously large. In length it reached from the second to the eighth rib, and across the base of the ventricles it measured six inches. The left ventricle was moderately hypertrophied, and very largely dilated. The mitral valve was healthy, and the aorta was slightly thickened, and moreover had suffered rupture of a peculiar kind; one of its septa was torn away from its attachments, and thus two of its pouches were reduced to a single irregular one. The right ventricle was dilated, but both the auricles preserved their natural states. In the ascending aorta and in its arch there were atheromatous deposits. The liver was very large, and the spleen and the kidneys were healthy."

How, then, did this medical accident set up this chemical disease?

The aortic valves bear the pressure of the whole column of the blood, and resist the tension of the arterial textures. Consequently the highest pressure of each ventricle-full of blood that comes into the arteries is exerted on these valves. As soon as they are broken the pressure falls on the interior of the ventricle, and this being much less resisting than the structure of the valves, dilates; and hence throughout the whole arterial system a state of lessened tension of blood, and consequently of lessened pressure of the arteries on the blood, is produced; and if the left ventricle were as feeble as the auricle, the blood would hardly move in the small arteries, and passive congestion of the capillaries and then of the veins would soon follow from the rupture of the aortic valves.

But the heart reacts on the increased pressure. Quicker and stronger the muscular structure endeavours to drive the blood through the system. This increased action causes a greater supply of blood to the muscular structure of the heart itself through the coronary arteries, which, contrary to other arteries, receive blood freest and easiest when the heart is most dilated during the diastole. This increased supply of blood and increased function give rise to hypertrophy, and when it is established this hypertrophy increases the force with which the blood circulates through the vessels, whilst the dilatation

increases the quantity of blood sent forward at each systole of the heart. Thus, the tension in the small arteries again may reach the amount that prevents congestion of the blood in the capillaries and in the veins.

Before this compensation can be reached, the diminished tension in the small arteries allows the blood to stagnate in the capillaries and in the veins; as the tension in them increases the watery part of the blood, or even this with fibrin diffuses from the increased pressure into the textures, and a more or less resisting œdema of the cellular tissue is thus produced. This œdema may exist in all the textures, and the obstructed circulation may give rise to diminished chemical actions of oxidation and nutrition; this alteration is most apparent when the obstruction takes place in any of the secreting organs. When in any secreting organ diminished pressure arises in the small arteries, increased tension is caused by the stoppage in the veins. The capillaries from which the secretion takes place become distended, the supply of oxygen and of substances from which the secretion is formed becomes insufficient for the formation of healthy secretion; altered and less oxidized products form; constituents of the blood unchanged may escape on the free surface of the gland, and generally quantitative and qualitative chemical errors in the products of the glands occur. Thus, for example, in the kidneys the congestion from heart disease may cause slightly albuminous urine or even fibrinous liquor sanguinis to pass into the urine; or with extreme pressure, blood-globules may be forced through.

Thus the whole chemistry of oxidation, nutrition, and secretion may be entirely changed by the pressure produced by a mechanical accident—so changed that even mortification may in extreme cases occur. Such was not the course of events in the patient with ruptured aortic valves. The heart did its best to enlarge and to strengthen itself, but the tension in the veins and the stoppage in the capillaries was too great a weight for it to overcome. Effusion of fluid in the extremities and in the pleura came on, and the mechanical obstruction and the chemical want of action soon put an end to his sufferings.

In the 'Transactions of the Pathological Society,' vol. x., p. 92, you will find another case reported by Dr. Peacock. "The left angle of the posterior segment of the aortic valves was torn from its attachment so as to allow the edge of the valve to be retroverted and free regurgitation to take place from the aorta into the ventricle. The heart was large, weighing twenty-three ounces avoirdupois. The cavity of the left ventricle especially was considerably increased in size, and its walls were thicker than natural. He died three months and a-half after the accident which ruptured the valve, of extreme dyspnœa. The lungs were found congested, œdematous, and very sparingly crepitant throughout."

The slow mechanical disease which will furnish me with a good illustration of the production of secondary chemical disease is vesicular emphysema of the lung. This is caused by the mechanical dilatation, perforation, and obliteration of the pulmonary membrane of the air cells by the jerking force of coughing, which presses at the same time equally downwards as well as upwards.

As the emphysematous cavity enlarges the air cells that were broken up to form it disappear, and hence the amount of membranous surface is lessened through which the process of oxygenation and decarbonization of the blood and textures is carried on. A great diminution of the amount of capillary vessels in the lungs is thus produced, and the quantity of blood that comes to be aërated is thus diminished, and the resistance to the circulation in the pulmonary artery is increased.

This resistance acts immediately on the right side of the heart, and tends to, and ultimately produces, dilatation of the right side of the heart. The slightest impediment in the right side of the heart acts immediately on the systemic venous system, causing first increased tension of the veins, then obstruction, and finally dropsical effusion.

In health the air cells are distended with elastic gases, and the pulmonary membrane is pressed inwardly by the direct weight of the atmosphere, and outwardly indirectly by the pressure on the ribs and abdomen. The elasticity of the lungs is equal to a column of mercury about one-fourth of an

inch high; this elasticity, with the weight of the air on the abdomen and ribs, gives a slight pressure resisting the dilatation of the air cells. Cough consists in the sudden more or less violent pressure on the air in the tubes and cells by the contraction of the diaphragm and muscles of the chest and the muscles of the bronchial tubes and trachea, the larynx being closed. This sudden contraction increases the pressure of the air on all parts of the vesicular structure of the lungs, and by long-continued, often-repeated mechanical pressure, the elasticity of the cells is lost where there is least resistance, and the pressure of the air in the vesicles more or less rapidly causes dilatation and perforation and ultimate obliteration of the pulmonary membrane; for each mechanical cough whilst forcing part of the air out acts with an equal and opposite force upon every part of the air cells.

The dilatation and destruction of the cells necessarily occasions the destruction also of the capillaries on each side of the pulmonary membrane, and as the amount of obliteration increases, a mechanical obstruction to the passage of blood through the lungs is produced, and by this the chemical process of the aëration of the blood is impeded. In consequence of the mechanical injury, the absorption of oxygen and the escape of carbonic acid may ultimately be reduced to such an extent that the whole blood may become more venous than arterial, and general loss of power from imperfect oxidation and general loss of substance and alteration in chemical composition from imperfect chemistry of nutrition may result.

Moreover, the mechanical impediment to the passage of the blood through the lungs increases the tension of the blood in the veins, and congestion, dilatation, and effusion may be caused throughout the venous system. Dropsical effusion in the textures occurs, not because the left side of the heart fails to send the blood through the veins as in insufficiency of the aortic valves and in dilatation of the left side of the heart, but because the right side of the heart cannot empty itself, even though sometimes by its increased action it ruptures the blood-vessels of the lungs in its endeavour to overcome the obstruction that exists in them. General suboxidation and

subtrophic action are not the only chemical errors caused by vesicular emphysema of the lungs. The general venous congestion affects the chemical actions in the secreting glands. The passage of the sluggish blood through the liver is made more slow, and chemical derangements in the secretion of the bile result. The capillaries of the kidney become congested, and the secretion of urine is diminished and its composition changed; ultimately fatty liver and jaundice, and albuminous urine and fatty degeneration of the kidney and uræmia may result from the primary mechanical injury by which the vesicular emphysema of the lung was produced.

Whilst speaking of medical accidents, I must for a moment here allude to another large class which, as they are in their commencement chemical and not mechanical, therefore belong to the first part of this course of lectures. The vast subject of poisons may be comprised in this class of accidents. Poisons, according to their quantity and quality, suddenly or slowly act chemically on the body, and thus give rise to chemical and mechanical changes which sometimes cause the instantaneous stoppage of all action—that is, death; and sometimes produce the most protracted increased or diminished chemical and mechanical actions—that is, more or less acute or chronic disease. Almost every vegetable and mineral medicine which we use, when taken in sufficiently large doses, acts as a poison. Hence you will at once see how the full knowledge of these medical accidents by poison may give you clear ideas regarding the effect of medicines in promoting, or retarding, or modifying, the action of the mechanical and chemical forces that cause disease. But I must now leave this vast subject, of which I will endeavour to draw a most unfinished sketch in an appendix to this course of lectures.

And here, before I conclude, I must add one word of apology for so exclusively dwelling throughout this course of lectures on the chemical and mechanical actions of disease. I have done so because I could thereby obtain a degree of clearness and a connection of ideas which is very far beyond that which the present theory and practice of medicine, with

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its "vitality," "degeneration," and "phlogistic action," can offer. Moreover, even now the knowledge of the chemical and mechanical actions in the body is still in its infancy; but it daily grows, and will grow, stronger, broader, and deeper until it will carry away our present theories of medicine, and will bring us new materials for the construction of a perfect building, of which I have tried in this course of lectures to trace an outline.

The present wide-spread disbelief among medical men regarding the existing theories of disease and the mode of action of remedies, and the utter disagreement which so frequently exists between those who ought from the same therapeutical knowledge to adopt almost identical practice, and the complete wreck of all authority in physic, proves that the theory and the practice of medicine are now in a transition state; that the ground is being cleared for a new structure based on the theory of the conservation of energy. The science and practice of medicine will quickly advance to perfection as soon as the progress of the physical sciences enables us to obtain clear ideas of the action of each force, and of the relation of all the forces that exist in every substance within us and around us. As soon as we possess and can use this knowledge our profession will regain that union, that power, and that position which must of necessity be ours when we are able to advise with certainty upon the separate and conjoint action in the body of all the forces that bring good and harm to mankind.

APPENDIX.

BEING A SKETCH OF SOME OF THE THERAPEUTIC ACTIONS OF MECHANICAL AND CHEMICAL FORCES.

INTRODUCTION.

Perfect knowledge of the action of medicines can only be obtained when the action of each force in each medicine upon each force in each texture of the body can be estimated.

Hence this outline must be most imperfect and incomplete, but it may serve to indicate the direction in which future progress lies, and perhaps to give an earnest of the results which after years of research may be attained.

The law of the conservation of energy entirely does away with every supposition that food or medicine can create or annihilate any force. Food can create no new force, but can only transfer the energy that is latent in the different substances that are eaten or drunk, so as directly to increase or to diminish one or other or all of the actions that take place in the body; or to increase or to diminish the resistance to these different actions.

Medicines also, like food, can carry latent energy into each part of the body, and they may become active within by increasing oxidation, nutrition, secretion, motion, and sensation; or by their properties they may put a check upon these functions by increasing the resistance or by altering the conditions necessary for the conversion of latent energy into active force.

At the present time only the first sketch of the application of the law of the conservation of energy to the action of

medicines can be drawn. First, because our knowledge is as yet too imperfect; secondly, because the interdependence of the different forces that act within us renders the exact estimation of each very difficult; thirdly, because a most complicated system for regulating the different motions in the body exists in the nerves, so that the action of every force can be promoted or prevented by means of the circulation; and, lastly, because the actions of many medicines are themselves complex, having an opposite effect at different times or in different doses.

The healing art may be separated into two grand divisions —the one chemical, and the other mechanical.

From the first division the practice of medicine has arisen, and from the second, surgery.

The great functions of medicine are chemically to affect, qualitatively or quantitatively, first the working, and secondly the repair, of the organs and structures of the body.

As I have in the preceding course of lectures chiefly considered the processes of oxidation and nutrition, so here I shall now, for the purpose of clearness, dwell only on the chemical action of medicines as influencing oxidation and nutrition in the different textures of which the body is composed, although a multitude of other chemical actions may exist which I shall not attempt now to bring before you.

But, first, you must entirely banish from your minds the notion that diseases are catastrophes or separate entities to be destroyed within or to be ejected, like devils, without, by which a perfect cure only can be obtained; and you must more and more be fully possessed by the fact that all diseases are the increase or diminution or qualitative modification of the never-resting correlated forces which constitute life.

The oxidation and the nutrition that occur in the body are affected by medicines in at least two ways.

First, directly by the passage of the medicines into the different textures of which the body is composed; in these textures oxidation is promoted or retarded, and in these nutrition is assisted or prevented.

Secondly, indirectly by the action of the medicines on the nerves that regulate the circulation; whereby the flow of blood through the vessels is increased or diminished.

Although nutrition and oxidation in the body are dependent the one upon the other, and cannot be separated in action, yet to obtain some clearness in our ideas on the effect of medicines I shall separate them by dividing remedies—

1st, into those that promote or retard oxidation. A: Directly promoting oxidation within each particle of every texture. B: Indirectly promoting oxidation through the medium of the nerves acting on the heart and blood-vessels. C: Directly retarding oxidation. D: Indirectly retarding oxidation.

And, 2ndly, into those medicines that promote or retard nutrition. E: Directly promoting nutrition in each particle of every texture. F: Indirectly promoting nutrition through the medium of the nerves acting on the heart and blood-vessels. G: Directly retarding nutrition. H: Indirectly retarding nutrition.

Until lately we possessed no definite knowledge of the diffusion of medicines after they entered into the blood. We now know that crystalloid food or medicine passes through the walls of the capillaries and through the membranes of textures and through cell walls as readily as though no membrane intervened between the blood and the parenchymatous or intracellular fluid. According to the diffusive power of the crystalloid substances in the liquor sanguinis, and in the inter- and intra-cellular fluid, the same substance will be found in equal quantities in these different places. Hence, by dialysis, all crystalloid medicines act as directly on the textures as on the blood; and no crystalloid medicine can be limited in its action to the blood alone.

When the crystalloid substances enter the different textures, they act according to their chemical power; and according to the actions going on in the different textures, and even in different parts of the same textures; and according to the chemical and physical properties of the substances of which the different parts of the different textures are composed.

In addition to this direct action the diffusion of the medicine into the nerves that regulate the circulation leads to an indirect action upon the processes going on in the different textures. The increased or diminished action of the heart and the expansion or contraction of the small arteries lead to an immediate alteration in the circulation of blood through any part, and this promotes or retards the chemical circulation or the rate of diffusion from the capillaries into the extures.

Thus, not only are the actions of oxidation and of nutrition dependent the one on the other, but even the direct and the indirect actions of medicines upon oxidation and upon nutrition are also dependent the one on the other; although for clearness, as I have said, I shall endeavour in this sketch to keep these two actions as separate as I can.

PART I.

The first great division of medicines consists of those which directly or indirectly promote or retard oxidation.

A. Medicines that directly promote Oxidation.

1st. Iron is probably one of the most certain remedies we possess, and when used in right quantity and at the right time, it seems as though its progress could be watched and its benefit accurately determined by the improved colour of the blood.

When a soluble salt of iron is taken, in a few hours some part of it is converted into a sulphuret, or is reduced to the state of oxide in the bowels, and thus losing its solubility and power of diffusion, it is thrown out as perfectly useless as if it had never been taken.

Another part escaping precipitation remains dissolved, and passes in from seven to ten minutes, when the stomach is empty, into the urine, where it may be detected by the ordinary chemical tests, partly oxidized, if capable of oxidation; and this part also is of no use unless some local action of iron on the urinary passages or bladder is required.

A third part, instead of passing off in the urine, diffuses from the liquor sanguinis into every texture, and into the blood-globules and white corpuscles, making a greater formation of hæmoglobin, and thereby promoting that combination with protagon on which the production of new blood-globules depends.

These blood-globules exercise a chemical action on the oxygen of the air which the membrane of the air vesicles transmits, and they and the fibrin together appropriate the incoming oxygen and carry it to the capillaries, whence it must diffuse into each structure to support the oxidation which takes place everywhere.

Hence, speaking generally, the more iron we absorb, the

more blood-globules we form, the richer also the muscles become in hæmoglobin, and the more oxygen is taken to the capillaries, and the more oxidation proceeds in the tissues and in the blood.

2ndly. Oxygen itself, and still more ozone, may be considered as direct promoters of oxidation. From the time of Dr. Beddoes and Mr. Boulton to our own time, by inhalation or imbibition, these remedies have been used, but hitherto there has been no general recognition of their worth at all comparable to that which exists regarding the value of iron. Theoretically, ozone, if not oxygen, ought to be a most potent remedy in the treatment of diseases arising from suboxidation, but as yet the right mode of using these agents, except as fresh air, has not been discovered, and probably until some means is found of keeping up the continuous action of these gases no considerable benefit will follow their use as medicines.

3rdly. Alkalies furnish out of the body and in the body the most marked evidence of assisting in oxidizing actions.

Very many substances are included in the class of alkalies, and probably no two of them have the same degree of action, although all have a general resemblance. Different alkaline substances diffuse into the blood and into the textures at different rates, partly on account of difference in their power of diffusion, but partly also on account of the amount of similar substances already present in the tissues. Thus, for example, carbonate of soda, carbonate of potass, carbonate of lithia, and phosphate of soda will pass in and out of the textures at different rates, according to the amounts of these substances already present in the fluid that saturates these tissues. The greater the difference between the quantity of substance in solution on each side (inside and outside) of any membrane, the quicker will equilibrium by diffusion be produced, and the sooner will the greatest possible action of the substance be obtained; and when the equilibrium is produced no further passage of the substance through the membrane will take place.

In the first lecture I have given some account of the rate of passage of some alkalies into and out of the textures, and at pages 21 to 23 you will find how alkalies act on organic

substances out of the body; and from the experiments there related you will see that there is every reason to believe that alkalies within us also act most powerfully by directly promoting oxidation. Wherever they diffuse they chemically assist the action of the oxygen there, and ultimately lead to the formation of carbonic acid. Hence the most efficacious alkalies are those that pass in most readily, and can be taken in the least neutralized condition. Thus caustic alkalies are more potent than subcarbonates, and carbonates more potent than bicarbonates.

4thly. Chlorine, iodine, and bromine are substances closely related in chemical properties, and all promote oxidation in the body by taking hydrogen from water and thereby liberating oxygen. Thus these substances act even more strongly as oxidizers than oxygen itself acts. For example, solution of blue indigo may be exposed freely to the oxygen of the air without being oxidized; but on adding chlorine, iodine, or bromine to the solution, oxidation immediately occurs.

When combined with alkalies these substances have sometimes a very different effect from that which they possess when free, for iodine is to iodide of potassium as chlorine is to common salt. But, like common salt, iodide of potassium is decomposed by some organic acids; thus we see it is decomposed on the skin when used as a lotion or as an ointment, and thus hydriodic acid may be liberated in the textures, and this acid sets free iodine when air or free oxygen is in contact with it.* Hence, when the oxidizing action is certainly required, chlorine, iodine, and bromine should be used in the free state, and the combinations of these substances with alkalies will not always produce the same amount of action as the free substances themselves are able to effect. That the neutral compounds possess strong actions is well known in medicine, and the power even of common salt to form chemical compounds with the innumerable neutral substances that occur in the body, as, for example, the compounds of salt and urea and salt and sugar, makes it probable that the iodides and

* See 'Annales de Chimie,' March, 1866, p. 376. M. Payen on Iodide of Potassium.

bromides, wherever they penetrate, act chemically (though not as oxidizers always) on a multitude of organic and inorganic substances with which they come into contact.

5thly. Nitrates, chlorates, permanganates, and iodates are occasionally given on the supposition that they liberate oxygen in the body; but there is as yet no proof that any of these substances can give rise to an increase of oxidation in the textures. Alkaline permanganates and nitrate of silver are so rapidly decomposed on touching any organic substance, that they must be deoxidized long before they can pass out of the blood into the textures. The permanganate of potass can scarcely have passed the lips before it has given up part of its oxygen to the mucus of the mouth. Hence, probably, excepting the iodates, the efficacy of all these substances is quite independent of their chemical power as oxidizers.

6thly. Many other substances when taken in any quantity have a strong chemical action—for example, salts of zinc, salts of copper, salts of antimony, and salts of mercury; of all these, the salts of mercury are the most remarkable on account of the use that has been made of them in the treatment of almost every disease in England. Salts of mercury belong to the class of irritant poisons; substances that act chemically on the organic matters with which they come in contact, causing increased chemical action. The more soluble the preparation, the more violent the action on the different organic and inorganic substances with which it comes in contact. The solubility of corrosive sublimate in a solution of albumen, and the solubility to a slight degree of calomel in common salt or in some of the many organic and inorganic substances it meets with in the stomach and bowels, is the cause why these substances are capable, the one quickly, the other slowly, of passing into every texture of the body, and when there, the same increased chemical action takes place as we see occurs in the gums as the earliest sign of the constitutional affection by mercury. This increased chemical action cannot occur without increased chemical oxidation taking place in the same part at the same time. So that mercury salts, instead of stopping inflammation, actually

cause increased oxidation, and the efficacy of mercurials in inflammation depends on a power of exciting the secretions and of irritating the mucous membrane from the stomach downwards, by which the bile is made to pass into the duodenum and mucus into the intestine, and on a chemical action on fibrin and albumen which stops the coagulability of the liquor sanguinis, and renders effused fibrin less cohesive, and so more easily removed by absorption, than it otherwise would be. Its reputation as an antiphlogistic probably is greatly due to its combination with opium, of which it corrects the chief inconveniences—namely, stoppage of the action of the liver, bowels, and other organs.

7thly. Many organic substances—as, for example, croton oil, castor oil, elaterium, ipecacuan, jalap, aloes, and many others—contain some oily or extractive matter, which acts on the outer or inner skin, and when absorbed gives rise to increased chemical action, whence comes heat and oxidation, and more rapid circulation and quicker nutritive changes. If the increased chemical action rises to a sufficient height, then the increased circulation causes mechanical obstruction and congestion, and inflammation is the final result.

8thly. Counter-irritation must be considered as an oxidizing action. The simplest example is friction, which not only acts by promoting mechanically the circulation of the blood, but the increased heat from the mechanical action gives rise to increased molecular change; in other words, to increased chemical action. External heat in all its different methods of application or production—as, for example, poultices, fomentations, water-dressings, flannels, cottons—acts in the same way as an equivalent amount of mechanical action would do. Increased thermal action cannot exist without giving rise to increased molecular action.

Electricity differs from mechanical, thermal, or photal motion in its capability of passing into each texture according to its conductivity or resistance. Hence this form of motion may penetrate far deeper into different structures and affect actions in parts of the body far beyond the reach of mechanical or of thermal force.

B. Medicines that indirectly promote Oxidation.

The causes that determine the force and frequency of the heart's contractions are so many and so complicated that it is with the greatest difficulty that the effect of medicines on the circulation can be determined by experiment.

Among these causes are, first, the action of the nerves; secondly, the action of the muscular structure itself; and thirdly, the chemical and mechanical quality and quantity of the blood, and its relative proportion to the system of vessels in which it is contained.

The present state of our knowledge regarding the influence of the different nervous systems upon the circulation shows that at the centre and probably also at the periphery a highly-complex nervous action, partly stimulating and partly checking the contractions of the heart and vessels, takes place.

That a stimulating and a checking action of the nerves on the heart exists, and is in the highest degree complex, is evident from the following facts:—

1st. The heart, at least in cold-blooded animals, when removed from the body goes on beating. Hence there must exist in the heart itself a centre of rhythmical action, the seat of which must be placed in the ganglionic cells which are disseminated through the heart's substance.

2ndly. On cutting the cervical portion of the ninth pair of a warm-blooded animal, the frequency of the heart's pulsations is remarkably increased, and on tetanising the extremity of the nerve, which is still by its cardiac branches in connection with the heart, its motion is slackened, and may even easily be stopped altogether. Hence the ninth pair must be regarded as the heart's inhibitory nerves.

The inhibitory action can also be exercised through the same nerves by stimulating the parts of the brain between the calamus scriptorius and the corpora quadrigemina from which these nerves arise, and this leads to the conclusion that there exists in this part of the brain a centre which incessantly controls by means of the ninth pair the rhythmical action of the centre in the heart itself.

But the perfection of the machine and the complexity of the nervous action do not end here.

3rdly. The action of the heart may also be stimulated by tetanising the cervical portion of the sympathetic nerve, and hence there is reason to believe that there is somewhere in the upper part of the spinal marrow a stimulating centre connected by the sympathetic fibres with the ganglionic cells of the heart.

4thly. On the other hand, experiments on the heart of cold-blooded animals removed from the body can only be explained by the assumption of an inhibitory centre, situated in the septum atriorum (or common substance of the two auricles in frogs). Thus, then, there exist at least four different centres of nervous action:—A stimulating (or musculo-motory, as it is called) centre in the heart, and an inhibitory centre there also, and these counteract each other. Then there is a similar pair of centres in the brain and spinal marrow, connected, apparently, with the corresponding centres in the heart by two sets of nerves, the ninth pair and the sympathetic.

A poisonous agent may be carried to and act on any of these four centres, and thereby stimulate or check the heart's motion. Thus, for example, digitaline does not act upon the heart itself or on the nerves in the heart, but upon the inhibitory centre in the brain; its effect is produced through the ninth pair, for when these are cut digitaline does not act.

Still further complicating the nervous action, the inhibitory centre in the brain is in connection with the sympathetic nerve, so that the action of the heart can be stopped by reflex action of the sympathetic nerve. Thus Bernstein has shown that when the two trunks of the sympathetic nerve in the abdomen are isolated (as can easily be done in the frog) and tetanised, the heart is seen to stand still as long as the ninth pair are entire.

As the sympathetic nerve and the ninth pair regulate the action of the heart, so the same power of contracting and relaxing the muscular fibres of the blood-vessels in the sublingual salivary glands, according to the experiments of

Claude Bernard, is exercised by the sympathetic nerve and the chorda tympani.

If the filaments of the sympathetic nerve alone as they enter the gland are tetanised, a highly-concentrated saliva is secreted, and the blood flows out of the gland of a dark colour. If, on the contrary, the chorda tympani alone be tetanised, saliva is secreted copiously, containing no great proportion of solid matter, whilst the blood that flows out of the gland is brightly coloured, like arterial blood, and sometimes the arterial impulse can be distinctly traced beyond the gland into the veins.

These results, so far as the colour of the blood and the abnormal pulse in the veins, can only be explained by assuming that the small blood-vessels in the gland are caused to contract by tetanising the sympathetic nerve, and that they are caused to dilate by tetanising the chorda tympani.

It is possible that a similar arrangement prevails throughout the whole circulatory system, but hitherto the existence of nerves which cause the vessels in general to contract has alone been demonstrated.

The consideration of the causes that disturb the circulation becomes still more complicated when the power of the muscle itself and the action of the fluid that circulates in the vessels and the resistance at the periphery have to be taken into account.

The power of the muscle itself may be affected by medicines, by nutrition, or by resistance. For example, it is most probable that veratrine stops the action of the heart in a totally different manner from digitaline, by affecting the muscular structure of the heart itself without the intervention of the nerves.

Moreover, the quantity of the blood and the average or total pressure which exists in the whole or in a part only of the circulation have been proved materially to affect the heart's power and frequency of action. Whenever an abnormal resistance is set up in any part of the system, as is, for example, the case in so many of the affections of the different textures of the kidney comprised under the name of Bright's

disease, the action of the heart is increased, just as the action of any voluntary muscle has been recently shown to be increased, by adding to the weight it has to lift; and whenever the proportion which the bulk of the blood should normally bear to the capacity of the vascular system is altered by the contraction of the small arteries, the increase of average pressure thus produced increases the frequency of the pulsation of the heart, as Ludwig and Thiry have demonstrated.

By chemical or mechanical action upon one, or more than one, of these different nervous or muscular centres of force, medicines may increase the frequency or the force of the contractions of the heart. In consequence, the blood will be sent more quickly through the capillaries, and greater rapidity of chemical circulation (diffusion) through the different textures will be produced, and from this increase of oxidation and of nutrition will arise.

Dr. Traube's experiments on the effects of digitaline, nicotine, oxide of carbon, curare, and antiarin all show the exceeding complexity of the action of these substances upon the heart; but from such experiments we shall obtain the data for rightly estimating the action of remedies on the nerves, and through them on the processes of oxidation and nutrition.

C. Medicines that directly retard Oxidation.

In this class are included that most important list of remedies which formerly constituted the medicinal part of the antiphlogistic treatment.

1st. Vegetable salines and dilute organic and mineral acids. These constitute the most directly-acting remedies for fever and inflammation which we possess.

The oxidation of vegetable salines I have brought before you in the fourth lecture, page 90.

The effect of organic and mineral acids in so checking oxidation as to cause even the accumulation of fat is mentioned in the ninth lecture, page 176 to page 178.

The first action of dilute mineral acids, when the stomach is quite empty, is on the mucous membrane and on the muscular structure; the nerves are not affected by dilute acids. When taken in the very small doses usually given, the alkalescence of the blood must quickly prevent any continued action of the acid as such on the blood-globules, the secretions, or the textures; but, by however little the alkalescence of the blood is diminished, or the blood-globules destroyed, by so much must the process of oxidation in the textures be diminished also; and if very large quantities of mineral acids could be evolved anywhere, accumulation and formation of fat, and probably a saccharine condition of that part, would be produced. The action of phosphorus, arsenic, and antimony in producing fatty degenerations of the liver, kidneys, and pepsine glands of the stomach, and in stopping the liver from forming glycogen, may partly depend on the production of the acids of these substances in these different places.

Some organic acids, as, for example, oxalic acid, act quite as strongly in neutralizing alkalescence as the dilute mineral acids, and multitudes of these organic acids are formed in all the textures of the body, and that mineral acids and bile acids when in excess may even produce so-called fatty degeneration is rendered certain by the experiments of M. Kühne, Traube, Leyden, and Munk. Oxalic acid and the bile acids, in combination with alkalies, have also the power of stopping the muscular action of the heart, and bile acids also rapidly dissolve the blood-globules, and thus retard oxidation.

Even the syrup which enters into so many prescriptions must be considered in its action as equivalent to so much organic acid taken into the system, and temporarily at least neutralizing so much alkalescence in the blood and in the fluid with which every texture is imbued.

Vegetable acid salts have always been considered as antiphlogistic remedies, and when oxidized to carbonates they may assist in the removal of organic impurities in the blood and textures by ultimately adding to the alkalescence of the

liquor sanguinis, and thus promoting oxidation everywhere; but this action is entirely different from that of organic and mineral acids, which, by lessening the alkalescence of the blood, directly retard the process of oxidation.

2ndly. Preparations of lead. As acids are the antitheses of alkalies, so lead is the antithesis of iron. In the 'Proceedings of the Royal Society,' June 15, 1865, you will see some experiments on the rapidity with which, in guinea-pigs, salts of thallium pass into every texture, and can be shown to be present after six hours even in the crystalline lens. Whether lead passes at the same rate or to the same distance may be doubted, but at least it can be seen in the gums and be detected in the muscles of the forearm, and from this there is every reason to believe that lead-salts diffuse widely into each texture, and act there according to the chemical properties of the different textures and substances with which they come in contact.

The multitude of organic substances from albumen to sugar that are precipitated by lead-salts shows the innumerable chemical actions that they must occasion in the body. Probably they precipitate both the hæmoglobin of the blood-globules and muscles, and the protagon of the nerves and blood-globules. Certainly the most marked visible effect is produced on muscles, nerves, and blood-globules. Combinations are formed which prevent further change, so that an arrest of action in the formation of muscles, nerves, and blood-globules, takes place. From the affections of the muscles and nerves paralysis and pain are produced, and from the affection of the blood-globules anæmia results, and this causes diminished oxidation in the tissues, and hence accumulation of urates in the textures is apt to occur, and though acute or chronic gout may follow, yet the increased chemical action is usually insufficient to remove the deposit which the arrest of oxidation continues to produce.

3rdly. Oxide of carbon displaces the oxygen in the blood-globules and forms a stable combination with the substance of the red corpuscles which is not destroyed by oxygen. Thus, carbonic oxide stops the passage of oxygen into the blood and

causes the same symptoms of poisoning as are produced by the hindrance of oxygen from passing into the blood.

Sulphuretted hydrogen, H_2S, is decomposed by the ozone of the blood, the sulphur being precipitated whilst the hydrogen reduces the blood to a lower state of oxygenation. An excess of sulphuretted hydrogen destroys the hæmoglobin of the blood, and thus gives rise to a deficiency of oxygen in the circulation.

Arseniated and antimoniated hydrogen, H_3As, H_3Sb, have nearly the same action as sulphuretted hydrogen.

Phosphoretted hydrogen, H_3P, reduces the blood, becoming phosphorous acid, PH_3O_3, and producing asphyxia from want of oxygen.

Oxide of nitrogen, NO, acts in the same way as oxide of carbon, forming at first NO_2.

4thly. Sulphurous acid and hydriodic acid are direct deoxidizing agents, and though the first chemical actions they produce in the body may be able to produce heat and force in the body, yet soon the deoxidizing action tends to stop the changes of oxidation which are going on within. The well-known action of sulphurous acid on nitrous acid, in the manufacture of sulphuric acid, need not here be dwelt on. As the sulphurous acid takes oxygen from the peroxide of nitrogen or hydrogen, so hydriodic acid, when near a substance that easily parts with its oxygen, reduces it, and by this action these substances can retard the changes which may be taking place in the body; moreover, by neutralizing alkali and by attacking the blood-globules, these and other mineral acids retard oxidation, and, like phosphoric acid, they are capable of producing fatty degeneration.

5thly. Gallic acid and tannic acid are strongly deoxidizing agents. When in contact with alkalies, as in the blood, they are capable of taking oxygen even from the blood-globules. They probably have no action on the nerves or muscles, exciting no contraction of the muscular structure. The action of tannin in precipitating albumen and in forming indefinite compounds with the skin gives no explanation of its action in astringing the small blood-vessels. The property of gallic

acid as an astringent requires also fresh experiments for the explanation of its action.

6thly. Rest, general and local, for muscles and nerves, and cold, must be considered as means directly hindering oxidation.

The appearance of the arcus senilis first where the eyelid prevents the action of light, and the fatty accumulation in unused parts, are examples of the chemical effect of rest.

D. Medicines that indirectly retard Oxidation.

As in the causes that indirectly promote oxidation, so in those that retard oxidation, three different actions must be distinguished:—1st. An action on the nerves; 2ndly. An action on the muscles; and 3rdly. An action resulting from the quantitative and qualitative relationship of the blood to the vessels.

1st. On the checking or controlling influence of the nerves upon the action of the heart and the capillaries.

Of all the actions that can be produced by chemical agents acting in the body, this is the most remarkable for its rapidity and intensity.

The effect of so comparatively uncomplex a body as prussic acid (C_2NH) in bringing all action to rest is almost too rapid to be investigated experimentally; but the effect of more slowly-acting substances—as, for example, morphia—shows quite as distinctly the mode of action of some of the most important agents that can be employed as medicines.

If any extremely delicate test for morphia existed, it would probably be found to follow the same course in rapidity and extent of diffusion as quinine; when taken on an empty stomach, in less than fifteen minutes it would be detectable in the blood; and in every texture of the body it would reach its maximum in from two to three hours; whilst there it would act according to its chemical properties and the properties of the different textures with which it was in contact. In twenty-four hours it would greatly decrease, and in seventy-two hours, by diffusion or oxidation, it would entirely disappear.

What the chemical action of alkaloids on nervous matter may be is not yet determined. When applied directly to a nerve, ammonia is found to destroy immediately the electrical and all other actions which the nerve can produce: this may be some evidence of the kind of power which the large class of alkaloids possess in acting on protagon. Chemistry has hardly entered on this vast field of inquiry, although the researches of Kühne and Eckhard and others show that the effect of inorganic and organic acids, alkalies, neutral substances, and salts on nerve and muscle must be determined before any clear views of the action of remedies can be obtained.

As soon as the salts of morphia enter into every nervous filament a molecular motion between the protagon and salt of morphia probably takes place; the resultant substance must be far less sensitive, far less capable of other molecular motion, than before, and until the morphia is destroyed by oxidation or removed by diffusion the nerve cannot recover its former mobility.

All experiments lead to the supposition that different alkaloids affect different parts of the complex nervous systems in greater or lesser degrees. Strychnia will act chiefly on the medulla; curarine and conicine will act most on the motor nerves; atropine will paralyse the nerves that contract the iris, while essarine will paralyse the nerves that dilate the pupil. No experiments at present can reach the causes of these variations, and for them and for other alkaloids we must take the fact, and long for the explanation which chemistry will some day give.

The dry tongue, the stoppage of the secretion of gastric juice, bile, intestinal fluid, and of urine, the paralysis of the nerves that dilate the iris, the loss of mental and nervous power after morphia—all these actions are evidence of the effect of morphia in stopping all chemical action and in lessening oxidation by acting on the nerves which lessen the circulation of the blood.

In this way opium is one of the most potent antiphlogistic remedies we possess, and to it probably the calomel

and opium treatment of this century owes its great reputation.

Of all the remedies that control hæmorrhage probably opium is one of the most potent. This is effected by the same mechanism acting through the same nerves that indirectly retard oxidation.

2ndly. Medicines that lessen the action of the muscles. Rest and cold are the most potent agents that can be mentioned here. Salts of potass, ammonia, and lead, and probably salts of zinc and baryta, and perhaps in small doses salts of antimony and veratrine, digitaline, and nicotine, may have a direct action on the muscular substance, especially of the heart, rendering it less sensitive to nervous influence, and thus controlling its contractions and causing less active circulation, and thus indirectly retarding or stopping oxidation; but here also we must wait for further experiments before any clear ideas can be obained.

3rdly. The qualitative and quantitative relation of the blood to the vessels can chiefly be affected in a negative sense by local or general bleeding, by dilutions, and by evacuations.

If now, then, we discard the last lingering trace of the theory of phlogiston, according to the present state of knowledge the antiphlogistic treatment is the retardation of chemical action; and as oxidation is the chief of all the chemical motions going on in the body, the antiphlogistic treatment is the arrest of an excess of oxidation and of all the mechanical, chemical, and other actions which arise from it.

PART II.

In the second great division of medicines I place those substances that directly or indirectly promote or retard nutrition.

The chemical actions which are concerned in the formation of the multitude of organic substances of which the body is composed are far more complicated than those comparatively simpler chemical actions on which oxidation depends. If even now the different steps and processes, the helps and hindrances which affect the formation of carbonic acid and water in the body, are not yet determined, how much less able must we be at present to comprehend the chemical actions which take place in the formation of blood-globules, bone, muscle, nerve, &c.

Many of those medicines that promote or retard oxidation at the same time promote or retard nutrition. When they are present in excess they render the formation of different substances more easy; and when absent the chemical actions necessary for the formation of these substances are retarded or altogether stopped.

Our knowledge is so deficient regarding the way in which these actions are carried on that at present no clear view of the chemistry of the repair of the body can be obtained. Still the fact is certain that some food and some medicines are capable of promoting or of retarding the formation of different substances. To comprehend this for the present we must assume no vital force, but we must wait until the advance of chemistry enables us to determine all that belongs to chemistry in the process of nutrition. Then, and not until then, we shall be able, by deducting the chemical portion, to see clearly how much of the actions that determine the composition, form, and position of the different structures depend on any distinct and peculiar force; and to this residue the term vital force may then be given.

E. Medicines or Food that directly promote Nutrition.

It is not possible to draw any distinction between food and medicine ; for oxygen, and iron, and water, and common salt are as necessary food as starch and gluten or fat and albumen ; and increased supply of any substance that can enter into the structure of any tissue as surely promotes nutrition as increased supply of air increases oxidation.

The most remarkable example of increased nutrition by medicine is seen in the increased formation of blood-globules when iron is taken. The formation of hæmoglobin implies the formation of hæmatin, and without iron no hæmatin is produced, so that iron may be regarded as one food of the blood-globules. When it is absorbed in greater quantities than the ordinary food supplies, increased formation of hæmatin occurs, and in cases of anæmia this increased formation may be watched and stopped when it is considered that sufficient red-colouring matter has been produced.

The chemical process by which the iron helps to build up the hæmatin is quite as unknown to us as was a few years since the formation of urea or any other of the innumerable organic substances which chemistry is now able synthetically to construct; but that the metal itself and many of its salts will lead to the increased formation of new blood-globules is proved by the innumerable preparations of iron that are in use in medicine, no one of which can be said to have an undoubted superiority in the cure of anæmia.

Possibly, by giving ready-formed hæmatin or hæmoglobin, a more rapid formation of blood-globules will be obtained than when any other preparation of iron is given.

The second remedy I may mention is phosphate or carbonate of lime in promoting nutrition of the bones. In cases of rickets, by giving ivory shavings, by powdered bone itself, by calcined bone, by pure phosphate or carbonate of lime, increased formation of bony substance may be produced.

The third medicine is cod-liver oil. This remedy clearly shows the impossibility of distinguishing between food and

medicine. Its chief ingredients increase the deposit of fat in the cellular tissue, and this nutritive action on the adipose tissue differs in no respect from that which might be obtained by turtle, or cream, or olive oil. It is, however, quite certain that many substances besides oily matter exist in the cod-liver oil, and to these intermixed substances the cod-liver oil probably owes its medicinal repute. M. Chevreul has found no less than twenty-nine substances in mutton suet.

Fourthly, it is highly probable that other nutritive substances might be found which will specially promote the nutrition of particular textures, the more nearly in chemical composition the nutritive substance agrees with the texture to be nourished. Thus, in failing supply of the whole blood, the whole blood may be renewed by transfusion. In wasting muscle from exercise or other cause, meat may be the special remedy. Gelatine may perhaps supply the wasting cellular tissue, and even the highest of all textures, the brain and nerve substance, may perhaps be best restored by food of which these substances form a part. That phosphorus assists in the formation of protagon, as iron does in the formation of blood-globules, is far from any direct proof. Far less probability exists that phosphoric acid or the salts of phosphoric acid—as phosphate of iron, or phosphate of iron and strychnia—can be so decomposed, and the elements recombined in the body, that the phosphorus may promote directly the nutrition of the brain or spinal cord. Whatever good these medicines may do otherwise they can hardly be of use in helping the formation of protagon, either in the nervous substance or in the blood-globules. Phosphorus or phosphorus acid can be shown by direct experiments (see Lecture IX., pp. 174 and 175) to be oxidized into phosphoric acid; and hence the phosphoric acid of our medicines, though it may leave the iron or strychnia in great part to combine with soda and other alkalies, and may keep continually passing into a more or less basic salt, yet will never lose its oxygen by reduction, never be capable of combining with carbon and hydrogen to form that phosphorised oil which exists in the nervous substance. The worth or the worthlessness of phosphorus or

phosphates as nutriment for the nerves must be established by experiments which the chemist alone is capable of making.

F. Medicines that indirectly promote Nutrition by, 1stly, increasing the action of the heart, and, 2ndly, by lessening the resistance in the capillaries.

The different ways in which the heart has its action increased I have already brought before you in speaking of medicines that indirectly promote oxidation. The exceedingly complex nervous system which makes the human machinery so far more perfect than any made by hand, renders it almost impossible to rightly estimate the way in which and by which different medicines acting upon the different nervous centres can cause increased action of the heart. It is not less difficult also to determine accurately the probable action of medicines upon the different nervous centres in lessening the resistance in the capillaries.

Besides these nervous actions there is also the action on the muscle itself by medicines, and by the work which it has to do, and by the qualitative and quantitative variations in the fluid which circulates in the heart and vessels.

All these different actions lead to the same result, and that is, increased flow of blood to the part; and whatever cause produces a flux of blood to any structure, in that structure increased nutritive action will take place. The Hunterian experiment on the growth of the spur of the cock when implanted in the comb is momentarily repeated wherever, by mechanical and chemical or any other force, the quantity of blood brought to any part is increased. From corns to cancers increased flow of blood causes increased growth of healthy and diseased structures; and in whatever way increased supply of blood to any part is occasioned, increased nutrition of that part or texture indirectly is produced.

Increased flow of blood to any part may be produced in at least four different ways by medicine.

First, there may be an action on the nerves which increase the action of the heart.

Secondly, there may be an action on the muscular structure of the heart itself.

Thirdly, there may be an action on the nerves that dilate the capillaries.

Fourthly, the quantity and quality of the blood in the heart and vessels may be improved, so that a smaller quantity may become equivalent to a larger quantity.

1st. Alcohol, ether and chloroform, nitrous oxide, chloride of methyl, olefiant gas, before they are destroyed by the oxidizing process going on in the body, have a very decided action on the heart through the nerves. This action on the nerves does not proceed from the action of the blood-globules, because the symptoms appear before any blood-globules are destroyed, because animals with white blood are affected by anæsthetics, and because animals, as frogs, the respiration of which is with difficulty interfered with, are easily and strongly affected by these substances.

The protagon of the nerves is readily acted on by these substances, and it is this same protagon in the blood-globules * that causes them also to be attacked and dissolved by these stimulants.

The first action of these substances, then, is a chemical combination with one ingredient of the nerves—this is the primary stimulating action ; and as soon as this combination is formed the nerve is rendered less sensitive (perhaps by being made less capable of being acted on by oxygen than before), and until the foreign substance is removed by oxidation the nerve is checked in its action.

2ndly. Of all the medicines that stimulate the muscles, probably ammonia is one of the most remarkable. It has no exciting action on the nerves of motion, but almost immediately deprives them of the power of exciting motion, but it acts as an intense exciter to the muscles.

3rdly. Medicines that dilate the capillaries, according to

* 'On the Existence of Protagon in the Blood,' by L. Hermann ('Archiv für Anatomie und Physiologie,' 1866, p. 36).

M. Bernard, do so by paralysing the sympathetic, which constantly tends to close the capillaries. This dilatation may also be caused not only by dividing the sympathetic nerve, but by acting reflexly or directly on the cerebro-spinal nerves.

In the submaxillary gland the vessels are relaxed and saliva flows when the superior cervical ganglion of the sympathetic is cut, and when the lingual nerve is excited as by vinegar, or the chorda tympani is irritated. Curare paralyses all the motor nerves, and then secretion of saliva takes place.

4thly. Improvement in the quality of the blood is chiefly effected by iron and animal food; or the quantity in any part may be increased by friction or by any other force.

G. Medicines that directly retard Nutrition, either, 1st, by themselves entering into combination with the organic substances of which the textures are composed, by which the chemical changes that would otherwise occur are stopped, or, 2ndly, by the accumulation in the textures of any of the substances resulting from the chemical changes in the textures.

Among the many mineral substances which act in the first way lead is the chief, and probably zinc, silver, copper, arsenic, antimony, and even in some rare cases mercury, as, for example, in methyl-mercury, can also combine with either nerves, muscles, skin, or other textures, rendering them incapable of going through changes on which their action depends.

Among the substances which act in the second way must be included all the different products from each texture in their downward course to carbonic acid, ammonia, water, and salts.

Even the accumulation of "ashes" may come to be impediments to the chemical changes on which nutrition depends, the old textures may cease to be removed, and "calcareous degeneration" may result.

When carbonic acid accumulates in the blood and textures from the pressure of more than four per cent. of carbonic acid in

the air, it causes no convulsions, provided sufficient oxygen is at the same time supplied ; but the carbonic acid passes from the blood to the nerves, and acts on the moving and on the regulating systems of nerves. At first the pressure of the blood is increased, and the frequency of the pulse becomes greater; then the regulating action prevails, the pulse becomes slower and larger ; then the pressure sinks quickly and considerably. The regulating action is exhausted, and again the increase of pressure shows the excitement of the motor system remains. Soon the motor action in the medulla oblongata is lost, and that proceeding from the ganglia of the heart alone remains, and this gives only slight pressure, small and quick systole and diastole, and long intervening pauses. The action on the nerves of respiration brings the respiration as well as the heart to rest, less oxygen goes in, and more carbonic acid accumulates till the muscles stop.

With carbonic oxide the same phenomena are produced with the addition that an immediate action of carbonic oxide takes place on the hæmoglobin of the blood-globules, and probably also on the hæmoglobin of the muscles (Virch. 'Archiv,' 1865). Carbonic oxide takes the place of the oxygen and hinders the escape of carbonic acid, so that not only a deficiency of oxygen, but an accumulation of carbonic acid is produced by it, the blood-globules being made incapable of carrying on the escape of carbonic acid from the textures (Pokrowsky, 'Archiv für Anatomie und Physiologie,' 1866, p. 59).

The organic acids are at least one step nearer than carbonic acid to the textures ; and if these acids accumulate in excess in the blood and textures, stoppage of oxidation and nutrition results.

Of all organic acids, the bile acids, even when combined with soda, have been proved by Kühne, Traube, and Hermann to have this action most decidedly, rapidly causing "fatty degeneration," dissolving the hæmoglobin, so that this constantly appears in the urine, and stopping the muscular action of the heart.

Other organic acid salts, as lactic, citric, tartaric, for the

time they remain in the textures before they are thrown out or burnt, stop the changes going on in the textures, and thus retard nutrition.

Sugar or fat, when taken in quantity, not only may lead to excessive deposit of fat, but may stop the changes in the material that is being removed to allow of new matter taking its place; and thus these substances may produce an arrest of nutrition, even whilst adding to the adipose deposit.

The nitrogenous substances that arise from the albuminous textures if they accumulate may react also in stopping nutrition; in addition to a multitude of other chemical actions on different textures which these substances may possess. What the amount and nature of these substances may be, and what the difference of their actions, cannot at present be conjectured with any certainty.

Beginning with carbonate of ammonia, and then urea, there are substances like kreatinine, animal quinoidine, and higher compounds of carbon, all of which, if they could be given as medicine, would check the formation of the downward products from albumen, and thus would retard nutrition. What other actions these substances possess in first combining with nerves and muscles, and then rendering them less active as long as the combination lasts, must be worked out by the most careful experiments; and among the multitude of substances that may ultimately prove to be formed in the body from albumen, perhaps we shall find the same poisons which, when procured from vegetables, we know produce the symptoms that constitute some of the diseases to which man is liable. Even animal strychnia and morphia may, like indigo, quinine, starch, or cellulose, be formed in the body by some modification of the process of removal of the textures.

II. Medicines that indirectly retard Nutrition by lessening the action of the heart and increasing the resistance in the capillaries, by which actions the flow of blood through the textures is lessened.

Four different actions may be distinguished, by any of which nutrition may be lessened—first, by an action on the

nerves of the heart; secondly, by an action on the muscular structure of the heart; thirdly, by contraction of the capillaries in consequence of an action upon the sympathetic nerve; fourthly, by the reduction, quantitatively or qualitatively, of the state of the blood.

It is impossible at the end of this sketch to bring before you in any detail the progress of experimental inquiry abroad on some of these subjects. I can now do little more than give you the names of some of the substances and the kinds of action which they possess, and I must refer you to the original works for full details of the experiments that have been made except in the case of potash salts, which I shall take solely because it gives a good example of the progress that may be expected in therapeutical knowledge from scientific research.

A medicine may act in only one, or in many, or in all the different ways that I have mentioned, and practically there is rarely a limited action, for the medicine if a crystalloid passes into every structure, and acts according to the properties of the substances with which it comes in contact.

1st. Of the medicines that act on the nerves of the heart in stopping its action, and thus making the circulation of the blood slower, strychnia is one of the most remarkable. When applied directly to the heart, it acts on the vagi nerves, and lessens the frequency of the heart's action; and it acts also on the ganglia. Nicotine acts on the vagi nerves alone. Conicine stops all the action in the peripheral nerves without affecting the muscular contractility. Digitaline first stimulates, and then paralyses the regulating nerves, and then stops the action of the heart. Quinine first stimulates, and then lessens, the action of the motor nerves of the heart.

The difficulty of determining whether the retarded circulation depends upon an increase of the checking action of the nerves or upon a decrease of the motor action, whether in the heart itself or in the brain, is in many experiments exceedingly great; and, to add to the complication, a reflex action on the vagi nerves may produce the same effect as though

a poison had been applied to the vagi nerves in the heart itself.

Thus, as I have already said, mechanical irritation of the sympathetic nerve in any part of the abdomen may be reflected by the vagi nerves to the heart and stop its action. Of this the occasional effect of a sudden blow on the solar plexus, or of cold water when drunk, are familiar, though happily rare, examples.

2ndly. Of the medicines that act chiefly on the muscular structure of the heart, veratria may be taken as the most remarkable: it stops the contractility of the heart, and colchicine has probably the same action; both may also act on the muscular structure of the small arteries, and thus alter the circulation through the capillaries.

The effects of salts of potassium, compared with the effects of sodium salts, show that salts of potassium act very strongly on muscular contractility. When salts of potassium are injected into the blood, the pulse falls rapidly, and the pressure of the blood, when accurately measured, rises for the first few minutes and then falls, and if the injection is then repeated the heart stops beating.

A muscle, by the application of potassium salts, may be rendered unexcitable to the stimulus of electricity, and it may be restored by treatment with sodium salts. A nerve, also, when treated with potassium salt, loses much quicker its power of exciting contractions in a muscle than when a similar nerve is treated with sodium salt. Even a nerve of sensation, as in a tooth, may lose its power when treated with potassium salt.

So remarkable are the phenomena that even a similarity has been stated to exist between the action of potassium salts and digitaline.

Microscopic observation shows that chloride of potassium may affect the blood-globules, making them contracted and granular, while chloride of sodium has no action of this kind.

3rdly. Of medicines that act on the capillaries morphia is the most striking. It acts also on the nerves of the heart, first as a stimulant, and secondly as a strong retarder.

4thly. The blood is made less energetic in quality or quantity by bleeding, starvation, and excess of water; by lead salts and excess of acids, mineral and organic.

Finally. If you look for a moment to the second great division of the healing art, you will find that among other indications of treatment two principal objects always present themselves to the surgeon. These are MECHANICALLY to control the working and repair of the body. In other words, he endeavours, qualitatively or quantitatively, to regulate by mechanical means the oxidation and nutrition which take place in every structure of the body.

Of each of these actions I must limit myself to one striking illustration.

The surgeon promotes oxidation in croup by mechanically opening the trachea. He retards oxidation after mechanical or chemical injuries by bleeding, by cold, and by rest, by defence from irritating substances. He directly promotes nutrition by removing pressure, as in the operation for strangulated hernia, and he retards nutrition by pressure or ligature in cases of aneurism.

As in medicine, so in surgery; the actions of oxidation and nutrition are mutually dependent everywhere, and no separation of these two actions in any part of the body actually takes place; and although I have endeavoured in this sketch to bring each of them separately before you, I have done so only in order that I might at least give you a clear though most imperfect view of the two most important of the many chemical actions of medicines * which are now being worked out by experimental research. The progress of all accurate knowledge of the actions of medicines depends now on exact chemical and physical experiments, and by the

* Among these are the action of acid in the stomach for digestion; the action of pepsine and pancreatine, &c.; the action of charcoal as a deodoriser; the action of an increase or decrease of acidity in the urine for the prevention or cure of stone; the destruction of parasitic animals and vegetables on the skin; the defence of the skin from the action of oxygen and dust by lead and zinc paints; the neutralizing foul discharges by charcoal poultices, chlorine washes, nitrate of silver lotions; the destruction of tumours by caustics; and many other chemical actions might be mentioned.

perfection of these alone will the practice of medicine lose its doubts and difficulties and disagreements and deceptions, and become esteemed by all as the art that can confer the highest benefit upon mankind.

Instead of being as formerly blind wielders of heavy clubs that may cure the disease or kill the patient; or instead of being as at present "judicious" or injudicious "bottle-holders," physicians at some future time will estimate exactly the effect of the increased or diminished action of any one force upon all the other forces concerned in the production of general or local disease; and by adding to the resistance of one or more forces, or by liberating more energy by means of the powers that are latent in food and medicine, they will restore that equilibrium of action in the body upon which our health depends.

Those who wish for further information on the chemical actions of medicines will find it by the following references, for which I am indebted to Dr. Ludimar Hermann, of Berlin:—

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